

Page 1

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSPTAJRK1626

PASSWORD:

TERMINAL (ENTER 1, 2, 3, OR ?):2

* * * * * * * * * * Welcome to STN International * * * * * * * * *

NEWS 1 Web Page URLs for STN Seminar Schedule - N. America
NEWS 2 "Ask CAS" for self-help around the clock
NEWS 3 FEB 27 New STN AnaVist pricing effective March 1, 2006
NEWS 4 MAY 10 CA/CAplus enhanced with 1900-1906 U.S. patent records
NEWS 5 MAY 11 KOREPAT updates resume
NEWS 6 MAY 19 Derwent World Patents Index to be reloaded and enhanced
NEWS 7 MAY 30 IPC 8 Rolled-up Core codes added to CA/CAplus and USPATFULL/USPAT2
NEWS 8 MAY 30 The F-Term thesaurus is now available in CA/CAplus
NEWS 9 JUN 02 The first reclassification of IPC codes now complete in INPADOC
NEWS 10 JUN 26 TULSA/TULSA2 reloaded and enhanced with new search and display fields
NEWS 11 JUN 28 Price changes in full-text patent databases EPFULL and PCTFULL
NEWS 12 JUL 11 CHEMSAFE reloaded and enhanced
NEWS 13 JUL 14 FSTA enhanced with Japanese patents
NEWS 14 JUL 19 Coverage of Research Disclosure reinstated in DWPI
NEWS 15 AUG 09 INSPEC enhanced with 1898-1968 archive
NEWS 16 AUG 28 ADISCTI Reloaded and Enhanced
NEWS 17 AUG 30 CA(SM)/CAplus(SM) Austrian patent law changes
NEWS 18 SEP 11 CA/CAplus enhanced with more pre-1907 records

NEWS EXPRESS JUNE 30 CURRENT WINDOWS VERSION IS V8.01b, CURRENT MACINTOSH VERSION IS V6.0c(ENG) AND V6.0Jc(JP), AND CURRENT DISCOVER FILE IS DATED 26 JUNE 2006.

NEWS HOURS STN Operating Hours Plus Help Desk Availability
NEWS LOGIN Welcome Banner and News Items
NEWS IPC8 For general information regarding STN implementation of IPC 8
NEWS X25 X.25 communication option no longer available

Enter NEWS followed by the item number or name to see news on that specific topic.

All use of STN is subject to the provisions of the STN Customer agreement. Please note that this agreement limits use to scientific research. Use for software development or design or implementation of commercial gateways or other similar uses is prohibited and may result in loss of user privileges and other penalties.

* * * * * * * * * * STN Columbus * * * * * * * * * * *

FILE 'HOME' ENTERED AT 15:38:13 ON 18 SEP 2006

10790288.trn

=> file reg
COST IN U.S. DOLLARS

FULL ESTIMATED COST

| SINCE FILE ENTRY | TOTAL SESSION |
|------------------|---------------|
| 0.21 | 0.21 |

FILE 'REGISTRY' ENTERED AT 15:38:24 ON 18 SEP 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2006 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file
provided by InfoChem.

STRUCTURE FILE UPDATES: 17 SEP 2006 HIGHEST RN 907180-17-0
DICTIONARY FILE UPDATES: 17 SEP 2006 HIGHEST RN 907180-17-0

New CAS Information Use Policies, enter HELP USAGETERMS for details.

Effective September 24, 2006, Concord 3D coordinates will no longer
be available. Please contact CAS Customer Care
(<http://www.cas.org/supp.html>) if you have a need for 3D coordinates.

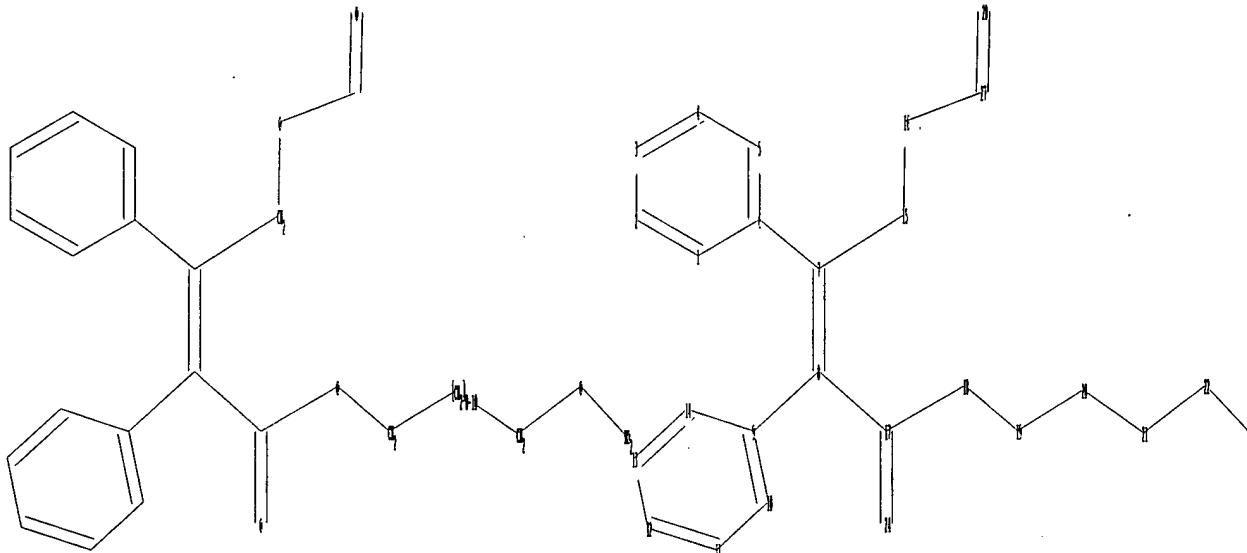
TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

Please note that search-term pricing does apply when
conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and
predicted properties as well as tags indicating availability of
experimental property data in the original document. For information
on property searching in REGISTRY, refer to:

<http://www.cas.org/ONLINE/UG/regprops.html>

=>
Uploading C:\Program Files\Stnexp\Queries\10790288\Struc 1.str



chain nodes :
7 8 15 16 17 18 19 20 21 22 23 24 27 28
ring nodes :
1 2 3 4 5 6 9 10 11 12 13 14
chain bonds :
6-7 7-8 7-15 8-9 8-17 15-16 16-27 17-18 17-24 18-19 19-20 20-21 21-22
22-23 27-28
ring bonds :
1-2 1-6 2-3 3-4 4-5 5-6 9-10 9-14 10-11 11-12 12-13 13-14
exact/norm bonds :
16-27 17-18 17-24 22-23 27-28
exact bonds :
6-7 7-8 7-15 8-9 8-17 15-16 18-19 19-20 20-21 21-22
normalized bonds :
1-2 1-6 2-3 3-4 4-5 5-6 9-10 9-14 10-11 11-12 12-13 13-14
isolated ring systems :
containing 1 : 9 :

Match level :

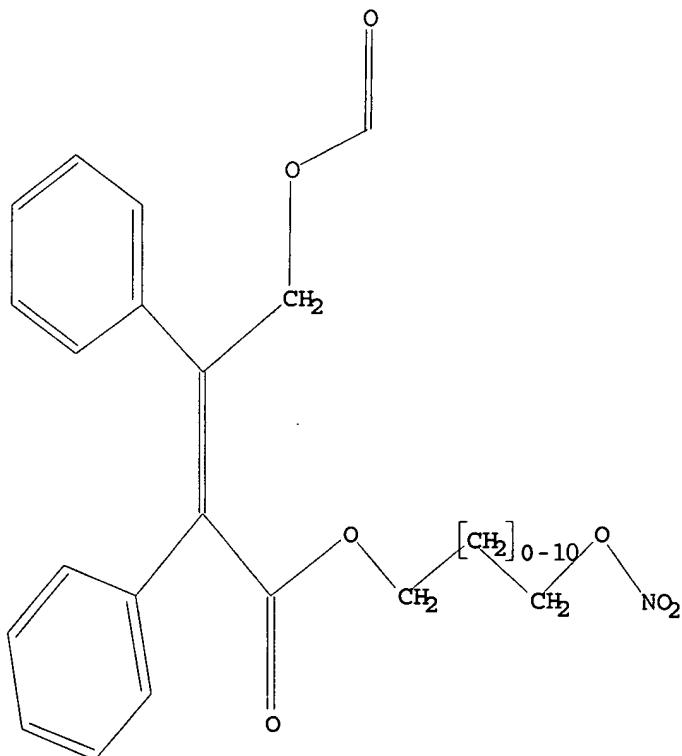
1:Atom 2:Atom 3:Atom 4:Atom 5:Atom 6:Atom 7:CLASS 8:CLASS 9:Atom 10:Atom
11:Atom 12:Atom 13:Atom 14:Atom 15:CLASS 16:CLASS 17:CLASS 18:CLASS
19:CLASS 20:CLASS 21:CLASS 22:CLASS 23:CLASS 24:CLASS 27:CLASS 28:CLASS

L1 STRUCTURE UPLOADED

=> d

L1 HAS NO ANSWERS

L1 STR



Structure attributes must be viewed using STN Express query preparation.

```
=> l1
SAMPLE SEARCH INITIATED 15:38:42 FILE 'REGISTRY'
SAMPLE SCREEN SEARCH COMPLETED - 1 TO ITERATE

100.0% PROCESSED      1 ITERATIONS          0 ANSWERS
SEARCH TIME: .00.00.01

FULL FILE PROJECTIONS: ONLINE **COMPLETE**
                        BATCH **COMPLETE**
PROJECTED ITERATIONS:   1 TO     80
PROJECTED ANSWERS:      0 TO     0

L2      0 SEA SSS SAM L1

=> l1 full
FULL SEARCH INITIATED 15:38:45 FILE 'REGISTRY'
FULL SCREEN SEARCH COMPLETED - 45 TO ITERATE

100.0% PROCESSED      45 ITERATIONS         6 ANSWERS
SEARCH TIME: 00.00.01

L3      6 SEA SSS FUL L1

=> file medline caplus
COST IN U.S. DOLLARS           SINCE FILE      TOTAL
                                ENTRY          SESSION
FULL ESTIMATED COST          166.94        167.15

FILE 'MEDLINE' ENTERED AT 15:38:53 ON 18 SEP 2006

FILE 'CAPLUS' ENTERED AT 15:38:53 ON 18 SEP 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

=> l3
L4      4 L3

=> d ibib abs hitstr 1-4

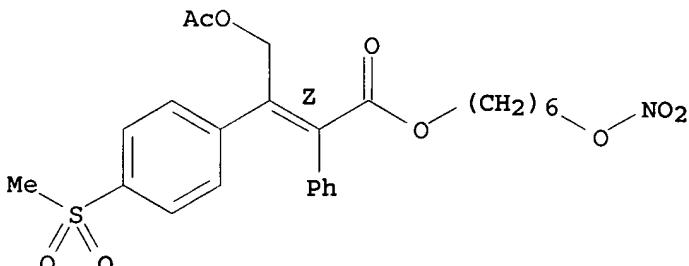
L4  ANSWER 1 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:14820 CAPLUS
DOCUMENT NUMBER: 144:260959
TITLE: Identification of a trace colored impurity in drug
       substance by preparative liquid chromatography and
       mass spectrometry
AUTHOR(S): Wang, Peng; Shi, Y.-J.; Helmy, Roy; Reamer, Robert;
           Vailaya, Anant
CORPORATE SOURCE: Analytical Research, Merck Research Laboratories,
                   Rahway, NJ, 07065, USA
SOURCE: Rapid Communications in Mass Spectrometry (2005),
        19(24), 3749-3754
CODEN: RCMSEF; ISSN: 0951-4198
PUBLISHER: John Wiley & Sons Ltd.
DOCUMENT TYPE: Journal
```

LANGUAGE: English
 AB 6-(Nitrooxy)hexyl-(2z)-4-(acetyloxy)-3-[4-(methylsulfonyl)phenyl]-2-phenylbut-2-enoate (enoate 1) was investigated as a novel therapy for pain relief. In a recent manufacturing run at the pilot plant scale, the enoate drug

substance was found to have a yellowish color not observed previously. An unknown impurity at trace level was detected by high-performance liquid chromatog. (HPLC) anal. and found to be the primary cause for the color of the drug substance. The colored impurity was enriched by preparative HPLC and structurally elucidated by liquid chromatog./tandem mass spectrometry (LC/MS/MS). It was found that the colored impurity was derived from the product of oxidative dimerization of rofecoxib, an impurity present in the enoic acid intermediate. It was further revealed by the photodiode array and LC/MS/MS data that the colored impurity exists in the drug substance as a pair of double-bond isomers with one isomer at majority. These findings were also confirmed by synthesizing the colored impurity through the proposed pathway.

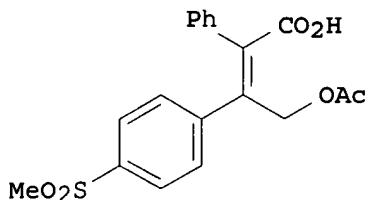
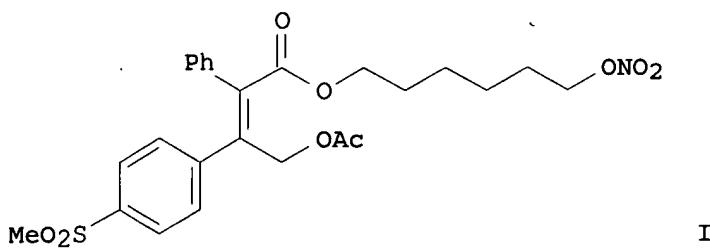
IT 754241-98-0
 RL: ANT (Analyte); THU (Therapeutic use); ANST (Analytical study); BIOL (Biological study); USES (Uses)
 (identification of colored impurity in drug substance by preparative HPLC)
 RN 754241-98-0 CAPLUS
 CN Benzeneacetic acid, α -[2-(acetyloxy)-1-[4-(methylsulfonyl)phenyl]ethylidene]-, 6-(nitrooxy)hexyl ester, (α Z)- (9CI) (CA INDEX NAME)

Double bond geometry as shown.



REFERENCE COUNT: 20 THERE ARE 20 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 2 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2005:1315893 CAPLUS
 DOCUMENT NUMBER: 144:212486
 TITLE: Synthesis of a NO-Releasing Prodrug of Rofecoxib
 AUTHOR(S): Engelhardt, F. Conrad; Shi, Yao-Jun; Cowden, Cameron J.; Conlon, David A.; Pipik, Brenda; Zhou, George; McNamara, James M.; Dolling, Ulf-H.
 CORPORATE SOURCE: Department of Process Research, Merck Company, Rahway, NJ, 07065-0900, USA
 SOURCE: Journal of Organic Chemistry (2006), 71(2), 480-491
 CODEN: JOCEAH; ISSN: 0022-3263
 PUBLISHER: American Chemical Society
 DOCUMENT TYPE: Journal
 LANGUAGE: English
 GI



AB A newly developed synthesis of a NO-releasing prodrug of rofecoxib is described. The highly productive process consists of five chemical steps and produces prodrug I in an overall 64% yield from com. available 3-phenyl-2-propyn-1-ol (II). The synthesis is highlighted by the carbometalation reaction of propargyl alc. II to generate the tetrasubstituted olefin core, sulfone acid III. Addnl., two alternate end-game strategies to prepare NO-COXIB I from this intermediate were explored and developed: (1) a convergent synthesis where a bromonitrate side chain is introduced in one step and (2) a two-step sequence that first installs the requisite six-carbon ester side chain followed by chemoselective nitration.

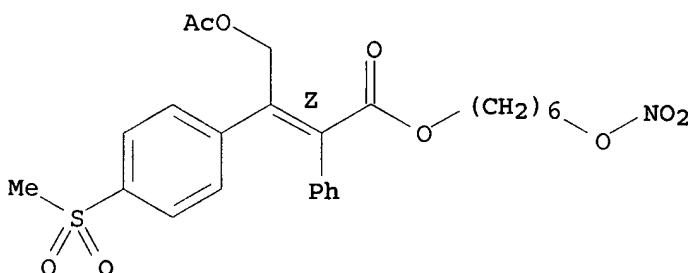
IT 754241-98-0P

RL: SPN (Synthetic preparation); PREP (Preparation)
(synthesis of a NO-releasing prodrug of rofecoxib in five chemical steps from 3-phenyl-2-propyn-1-ol)

RN 754241-98-0 CAPLUS

CN Benzeneacetic acid, α -[2-(acetoxy)-1-[4-(methylsulfonyl)phenyl]ethylidene]-, 6-(nitrooxy)hexyl ester, (α Z)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

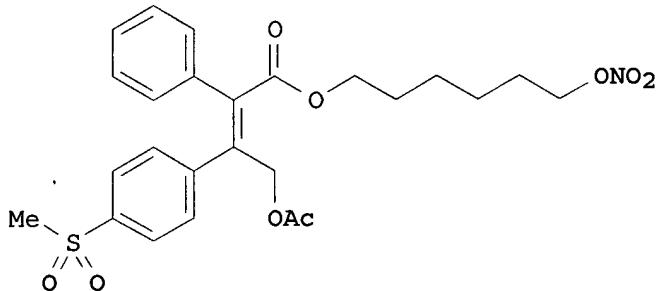


REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L4 ANSWER 3 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:963804 CAPLUS

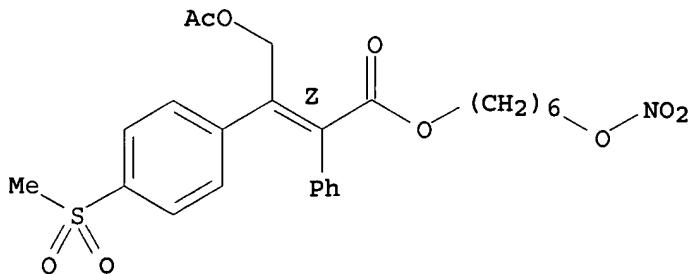
DOCUMENT NUMBER: 143:266677
 TITLE: Process for making nitric oxide releasing prodrugs of diaryl-2-(5H)-furanones as cyclooxygenase-2 inhibitors
 INVENTOR(S): Shi, Yao-Jun; Engelhardt, F. Conrad; Cowden, Cameron John; Conlon, David A.; Pipik, Brenda
 PATENT ASSIGNEE(S): USA
 SOURCE: U.S. Pat. Appl. Publ., 16 pp.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|----------------------------------|------------------------|
| US 2005192346 | A1 | 20050901 | US 2005-66676
US 2004-549126P | 20050225
P 20040301 |
| PRIORITY APPLN. INFO.: | | | | |
| OTHER SOURCE(S): | CASREACT 143:266677; MARPAT 143:266677 | | | |
| GI | | | | |



- AB The invention encompasses a novel process for making prodrugs of cyclooxygenase-2 selective inhibitors that convert in vivo to diaryl-2-(5H)-furanones and also liberate nitric oxide in vivo. As such, the compds. may be co-dosed with low-dose aspirin to treat chronic cyclooxygenase-2 mediated diseases or conditions, effectively reduce the risk of thrombotic cardiovascular events and potentially renal side effects and at the same time reduce the risk of GI ulceration or bleeding. I was prepared starting from 3-phenyl-2-propyn-1-ol and 4-thioanisole magnesium chloride, acetylation, and the intermediate converted to the carboxylic acid, the thio group oxidized to the methylsulfonyl derivative and reaction with 6-bromohexyl nitrate to give I.
- IT 754241-98-0P
 RL: SPN (Synthetic preparation); THU (Therapeutic use); BIOL (Biological study); PREP (Preparation); USES (Uses)
 (preparation of nitric oxide releasing prodrugs of diaryl-2-(5H)-furanones as cyclooxygenase-2 inhibitors)
- RN 754241-98-0 CAPLUS
- CN Benzeneacetic acid, α -[2-(acetoxy)-1-[4-(methylsulfonyl)phenyl]ethylidene]-, 6-(nitrooxy)hexyl ester, (α Z)- (9CI) (CA INDEX NAME)

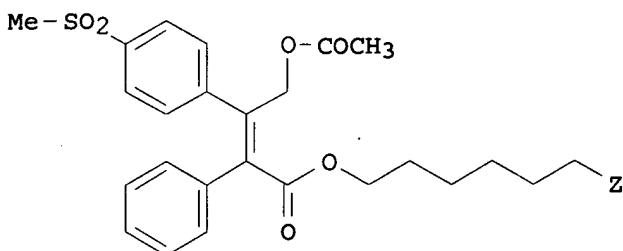
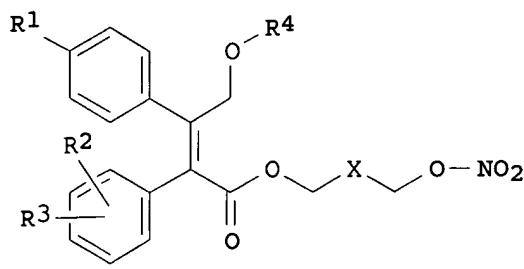
Double bond geometry as shown.



L4 ANSWER 4 OF 4 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2004:739958 CAPLUS
 DOCUMENT NUMBER: 141:260542
 TITLE: Preparation of nitric oxide releasing prodrugs of diaryl-2-(5H)-furanones as selective cyclooxygenase-2 inhibitors
 INVENTOR(S): Berthelette, Carl; Li, Lianhai; Sturino, Claudio;
 Wang, Zhaoxin
 PATENT ASSIGNEE(S): Can.
 SOURCE: U.S. Pat. Appl. Publ., 19 pp.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|------------|
| US 2004176331 | A1 | 20040909 | US 2004-790288 | 20040301 |
| AU 2004240700 | A1 | 20041202 | AU 2004-240700 | 20040301 |
| CA 2517490 | AA | 20041202 | CA 2004-2517490 | 20040301 |
| WO 2004103955 | A1 | 20041202 | WO 2004-CA314 | 20040301 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
TD, TG | | | | |
| EP 1601644 | A1 | 20051207 | EP 2004-761562 | 20040301 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK | | | | |
| PRIORITY APPLN. INFO.: | | | US 2003-452124P | P 20030305 |
| | | | WO 2004-CA314 | W 20040301 |

OTHER SOURCE(S): MARPAT 141:260542
 GI



AB Title compds. I [X = (CH₂)_n; n = 3-6; R₁ = SO₂Me, SO₂NH₂, SO₂NHCOCF₃, etc.; R₂, R₃ = H, halo, alkoxy, etc.; R₄ = CO-alkyl, CO(CH₂)_mNR₅R₆; m = 1-4; R₅, R₆ = H, halo-substituted alkyl] and their pharmaceutically acceptable salts were prepared. For example, O-alkylation of AgNO₃ by bromide II (Z = Br), e.g., prepared from Rofecoxib in 6-steps, afforded nitrooxyhexyl II (Z = -ONO₂). In human blood PGE2 inhibition production assays, nitrooxyhexyl II (Z = -ONO₂) exhibited an IC₅₀ value of 0.22 μM. Of note, the "unconverted prodrugs" of compds. I are inactive inhibitors of COX-1 and COX-2 activity. Compds. I are claimed useful for the treatment of cyclooxygenase-2 mediated diseases or conditions.

IT 754241-98-0P 754241-99-1P 754242-00-7P

754242-01-8P 754242-02-9P

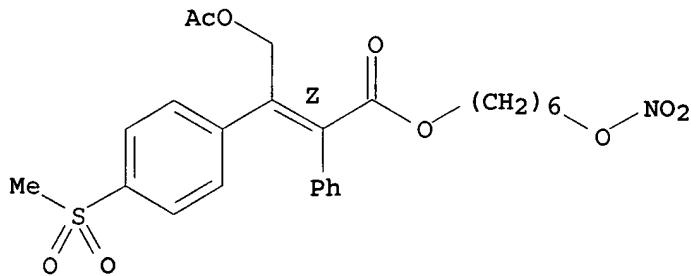
RL: PAC (Pharmacological activity); **SPN:** (Synthetic preparation); **THU:** (Therapeutic use); **BIOL:** (Biological study); **PREP:** (Preparation); **USES:** (Uses)

(preparation of nitric oxide releasing prodrugs of diarylfuranones as selective COX-2 inhibitors)

RN 754241-98-0 CAPLUS

CN Benzeneacetic acid, α-[2-(acetoxy)-1-[4-(methylsulfonyl)phenyl]ethylidene]-, 6-(nitrooxy)hexyl ester, (αZ)-(9CI) (CA INDEX NAME)

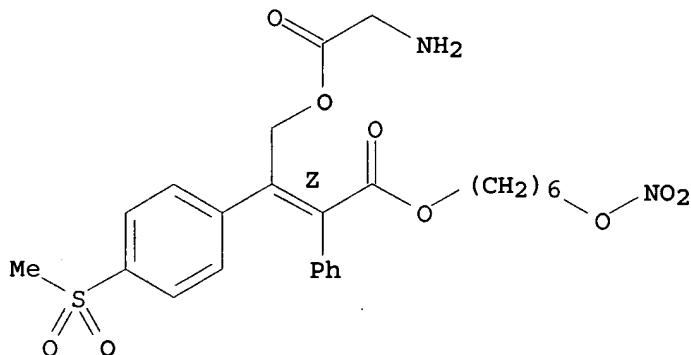
Double bond geometry as shown.



RN 754241-99-1 CAPLUS

CN Glycine, (2Z)-2-[4-(methylsulfonyl)phenyl]-4-[[6-(nitrooxy)hexyl]oxy]-4-oxo-3-phenyl-2-butenyl ester, monohydrochloride (9CI) (CA INDEX NAME)

Double bond geometry as shown.

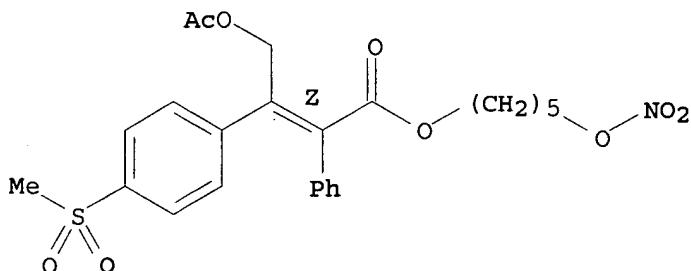


● HCl

RN 754242-00-7 CAPLUS

CN Benzeneacetic acid, α-[2-(acetoxy)-1-[4-(methylsulfonyl)phenyl]ethylidene]-, 5-(nitrooxy)pentyl ester, (αZ)-(9CI) (CA INDEX NAME)

Double bond geometry as shown.

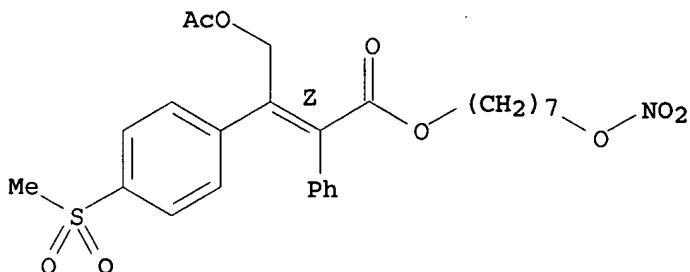


RN 754242-01-8 CAPLUS

CN Benzeneacetic acid, α-[2-(acetoxy)-1-[4-(methylsulfonyl)phenyl]ethylidene]-, 7-(nitrooxy)heptyl ester, (αZ)-

(9CI) (CA INDEX NAME)

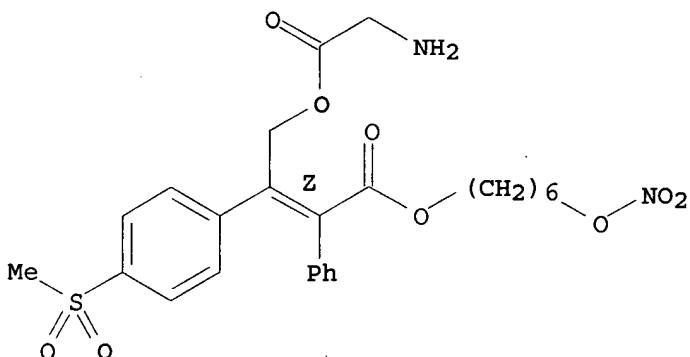
Double bond geometry as shown.



RN 754242-02-9 CAPLUS

CN Glycine, (2Z)-2-[4-(methylsulfonyl)phenyl]-4-[[6-(nitrooxy)hexyl]oxy]-4-oxo-3-phenyl-2-butenyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.



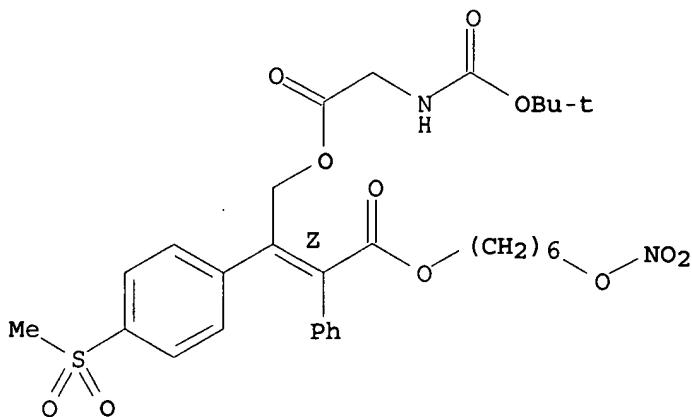
IT 754242-09-6P

RL: RCT (Reactant); SPN (Synthetic preparation); PREP (Preparation); RACT (Reactant or reagent)
(preparation of nitric oxide releasing prodrugs of diarylfuranones as selective COX-2 inhibitors)

RN 754242-09-6 CAPLUS

CN Glycine, N-[(1,1-dimethylethoxy)carbonyl]-, (2Z)-2-[4-(methylsulfonyl)phenyl]-4-[[6-(nitrooxy)hexyl]oxy]-4-oxo-3-phenyl-2-butenyl ester (9CI) (CA INDEX NAME)

Double bond geometry as shown.



| | | | |
|--|------------------|---------------|--|
| => file reg | | | |
| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION | |
| FULL ESTIMATED COST | 21.41 | 188.56 | |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION | |
| CA SUBSCRIBER PRICE | -3.00 | -3.00 | |

FILE 'REGISTRY' ENTERED AT 15:39:56 ON 18 SEP 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2006 American Chemical Society (ACS)

Property values tagged with IC are from the ZIC/VINITI data file provided by InfoChem.

STRUCTURE FILE UPDATES: 17 SEP 2006 HIGHEST RN 907180-17-0
DICTIONARY FILE UPDATES: 17 SEP 2006 HIGHEST RN 907180-17-0

New CAS Information Use Policies, enter HELP USAGETERMS for details.

Effective September 24, 2006, Concord 3D coordinates will no longer be available. Please contact CAS Customer Care (<http://www.cas.org/supp.html>) if you have a need for 3D coordinates.

TSCA INFORMATION NOW CURRENT THROUGH June 30, 2006

Please note that search-term pricing does apply when conducting SmartSELECT searches.

REGISTRY includes numerically searchable data for experimental and predicted properties as well as tags indicating availability of experimental property data in the original document. For information on property searching in REGISTRY, refer to:

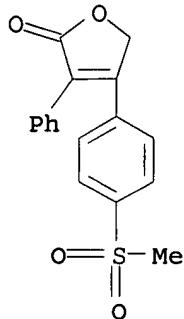
<http://www.cas.org/ONLINE/UG/regprops.html>

=> rofecoxib
L5 1 ROFECOXIB

10790288.trn

=> d str

L5 ANSWER 1 OF 1 REGISTRY COPYRIGHT 2006 ACS on STN



PROPERTY DATA AVAILABLE IN THE 'PROP' FORMAT

=> log h

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|--|------------------|---------------|
| FULL ESTIMATED COST | 6.58 | 195.14 |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |
| CA SUBSCRIBER PRICE | 0.00 | -3.00 |

SESSION WILL BE HELD FOR 60 MINUTES

STN INTERNATIONAL SESSION SUSPENDED AT 15:41:10 ON 18 SEP 2006

Connecting via Winsock to STN

Welcome to STN International! Enter x:x

LOGINID:SSPTAJRK1626

PASSWORD:

* * * * * RECONNECTED TO STN INTERNATIONAL * * * * *
SESSION RESUMED IN FILE 'REGISTRY' AT 15:47:23 ON 18 SEP 2006
FILE 'REGISTRY' ENTERED AT 15:47:23 ON 18 SEP 2006
COPYRIGHT (C) 2006 American Chemical Society (ACS)

| COST IN U.S. DOLLARS | SINCE FILE ENTRY | TOTAL SESSION |
|--|------------------|---------------|
| FULL ESTIMATED COST | 6.58 | 195.14 |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE ENTRY | TOTAL SESSION |

CA SUBSCRIBER PRICE 0.00 -3.00

=> d his

(FILE 'HOME' ENTERED AT 15:38:13 ON 18 SEP 2006)

FILE 'REGISTRY' ENTERED AT 15:38:24 ON 18 SEP 2006

L1 STRUCTURE uploaded
L2 0 L1
L3 6 L1 FULL

FILE 'MEDLINE, CAPLUS' ENTERED AT 15:38:53 ON 18 SEP 2006

L4 4 L3

FILE 'REGISTRY' ENTERED AT 15:39:56 ON 18 SEP 2006

L5 1 ROFECOXIB

=> file medline caplus
COST IN U.S. DOLLARS SINCE FILE TOTAL
FULL ESTIMATED COST ENTRY SESSION
DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) SINCE FILE TOTAL
CA SUBSCRIBER PRICE ENTRY SESSION

| | | |
|--|------------|---------|
| COST IN U.S. DOLLARS | SINCE FILE | TOTAL |
| FULL ESTIMATED COST | ENTRY | SESSION |
| | 6.58 | 195.14 |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE | TOTAL |
| | ENTRY | SESSION |
| CA SUBSCRIBER PRICE | 0.00 | -3.00 |

FILE 'MEDLINE' ENTERED AT 15:47:38 ON 18 SEP 2006

FILE 'CAPLUS' ENTERED AT 15:47:38 ON 18 SEP 2006
USE IS SUBJECT TO THE TERMS OF YOUR STN CUSTOMER AGREEMENT.
PLEASE SEE "HELP USAGETERMS" FOR DETAILS.
COPYRIGHT (C) 2006 AMERICAN CHEMICAL SOCIETY (ACS)

=> 15
L6 1523 L5

=> dup rem 16
PROCESSING COMPLETED FOR L6
L7 1521 DUP REM L6 (2 DUPLICATES REMOVED)

=> l7 and prodrug
L8 49 L7 AND PRODRUG

=> d ibib abs 1-49

L8 ANSWER 1 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2006:740188 CAPLUS
DOCUMENT NUMBER: 145:159849
TITLE: Methods and compositions using cyclooxygenase 2
(COX-2) inhibitors for the treatment of psychiatric
disorders, and combination therapies
INVENTOR(S): Muller, Norbert
PATENT ASSIGNEE(S): Germany
SOURCE: U.S. Pat. Appl. Publ., 34 pp., Cont.-in-part of U.S.
Ser. No. 157,969.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 3
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|------------------|-----------------|----------|
| US 2006167074 | A1 | 20060727 | US 2005-320757 | 20051230 |
| US 2003130334 | A1 | 20030710 | US 2002-157969 | 20020531 |
| EP 1627639 | A2 | 20060222 | EP 2005-24864 | 20020531 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| PRIORITY APPLN. INFO.: | | DE 2001-10129328 | A 20010619 | |
| | | US 2002-364904P | P 20020314 | |
| | | US 2002-157969 | A2 20020531 | |
| | | DE 2001-10129320 | A 20010619 | |
| | | EP 2002-738138 | A3 20020531 | |

AB A method for the prevention, treatment, or inhibition of a psychiatric disorder, in particular schizophrenia, is described which comprises administering a COX-2 inhibitor or prodrug thereof to a subject. Moreover, a method for the prevention, treatment, or inhibition of a psychiatric disorder, in particular schizophrenia or depressive disorders, is disclosed comprising administering to a subject a COX-2 inhibitor or prodrug thereof in combination with a neuroleptic drug or an antidepressant. Compns. and kits that are suitable for the practice of the method are also described.

L8 ANSWER 2 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2006:453900 CAPLUS

DOCUMENT NUMBER: 145:116702

TITLE: Racemic and chiral sulfoxides as potential prodrugs of the COX-2 inhibitors Vioxx and Arcoxia

AUTHOR(S): Caturlla, Francisco; Amat, Merce; Reinoso, Raquel F.; Cordoba, Monica; Warrelow, Graham

CORPORATE SOURCE: Department of Medicinal Chemistry, Almirall Prodesfarma S.A., Research Center, Barcelona, 08024, Spain

SOURCE: Bioorganic & Medicinal Chemistry Letters (2006), 16(12), 3209-3212

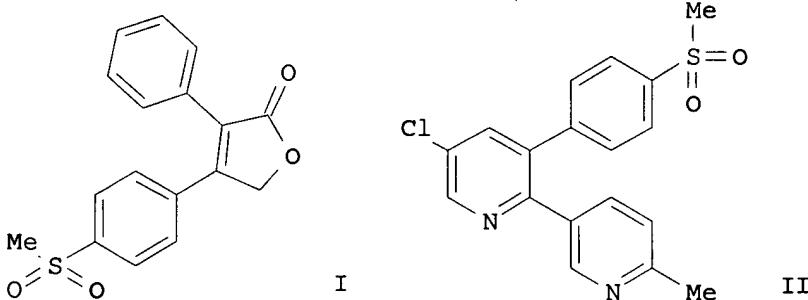
CODEN: BMCL8; ISSN: 0960-894X

PUBLISHER: Elsevier B.V.

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



AB The preparation of the sulfoxide analogs (I) and (II), and their enantiomeric pure forms is discussed as well as their potential to act as prodrugs to the potent and selective sulfone-containing COX-2 inhibitors rofecoxib and etoricoxib. Sulfoxides I and II were shown to be effectively transformed

in vivo into rofecoxib and etoricoxib, resp., after oral administration in rats. In the case of sulfoxide I, both a slightly improved pharmacokinetic profile and a better pharmacol. activity in an arthritis model were seen when compared with rofecoxib.

REFERENCE COUNT: 6 THERE ARE 6 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 3 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1315893 CAPLUS

DOCUMENT NUMBER: 144:212486

TITLE: Synthesis of a NO-Releasing Prodrug of Rofecoxib

AUTHOR(S): Engelhardt, F. Conrad; Shi, Yao-Jun; Cowden, Cameron J.; Conlon, David A.; Pipik, Brenda; Zhou, George; McNamara, James M.; Dolling, Ulf-H.

CORPORATE SOURCE: Department of Process Research, Merck Company, Rahway, NJ, 07065-0900, USA

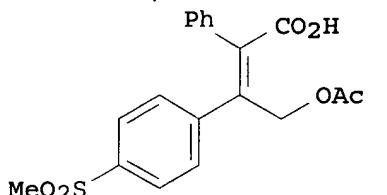
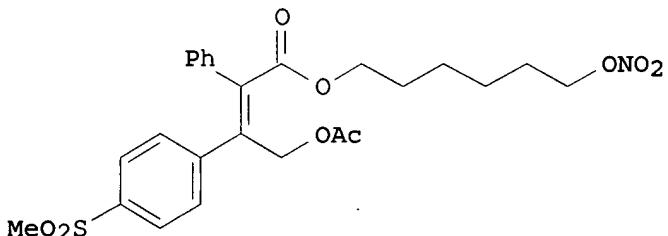
SOURCE: Journal of Organic Chemistry (2006), 71(2), 480-491
CODEN: JOCEAH; ISSN: 0022-3263

PUBLISHER: American Chemical Society

DOCUMENT TYPE: Journal

LANGUAGE: English

GI



AB A newly developed synthesis of a NO-releasing prodrug of rofecoxib is described. The highly productive process consists of five chemical steps and produces prodrug I in an overall 64% yield from com. available 3-phenyl-2-propyn-1-ol (II). The synthesis is highlighted by the carbometalation reaction of propargyl alc. II to generate the tetrasubstituted olefin core, sulfone acid III. Addnl., two alternate end-game strategies to prepare NO-COXIB I from this intermediate were explored and developed: (1) a convergent synthesis where a bromonitrate side chain is introduced in one step and (2) a two-step sequence that first installs the requisite six-carbon ester side chain followed by chemoselective nitration.

REFERENCE COUNT: 14 THERE ARE 14 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 4 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1294044 CAPLUS
DOCUMENT NUMBER: 144:17160
TITLE: Method using camptothecin compounds, pyrimidine derivatives, and antitumor agents for treating abnormal cell growth
INVENTOR(S): Denis, Louis J.; Compton, Linda D.
PATENT ASSIGNEE(S): Pfizer Inc, USA
SOURCE: U.S. Pat. Appl. Publ., 32 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| US 2005272755 | A1 | 20051208 | US 2005-145097 | 20050603 |
| WO 2005117980 | A1 | 20051215 | WO 2005-IB1527 | 20050523 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NG, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |

PRIORITY APPLN. INFO.: US 2004-577268P P 20040604
AB The invention discloses a method for treating abnormal cell growth in a subject, comprising administering to the subject (a) a compound selected from a camptothecin, a camptothecin derivative, or a pharmaceutically acceptable salt, solvate or prodrug thereof; (b) a pyrimidine derivative or a pharmaceutically acceptable salt, solvate or prodrug thereof; and (c) an antitumor agent selected from antiproliferative agents, kinase inhibitors, angiogenesis inhibitors, growth factor inhibitors, COX-1 inhibitors, COX-2 inhibitors, mitotic inhibitors, alkylating agents, antimetabolites, intercalating antibiotics, growth factor inhibitors, radiation, cell cycle inhibitors, enzymes, topoisomerase inhibitors, biol. response modifiers, antibodies, cytotoxics, antihormones, antiandrogens and combinations thereof.

L8 ANSWER 5 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:1291841 CAPLUS
DOCUMENT NUMBER: 144:40800
TITLE: Glucosamine and glucosamine/anti-inflammatory mutual prodrugs, compositions, and methods
INVENTOR(S): Capomacchia, Anthony C.; Garner, Solomon T., Jr.; Beach, J. Warren
PATENT ASSIGNEE(S): The University of Georgia Research Center Inc., USA
SOURCE: PCT Int. Appl., 83 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 2005116086 | A2 | 20051208 | WO 2005-US11739 | 20050407 |
| WO 2005116086 | A3 | 20060824 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,
NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL,
SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA,
ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
MR, NE, SN, TD, TG | | | | |

PRIORITY APPLN. INFO.: US 2004-560128P P 20040407

OTHER SOURCE(S) : MARPAT 144:40800

AB Mutual prodrugs of glucosamine, and derivs. and analogs of glucosamine and an anti-inflammatory agent, compns. thereof, and methods for, e.g., treating disorders and conditions by administration of the compns. are provided. Topical compns. of glucosamine, and derivs. and analogs of glucosamine are also provided.

L8 ANSWER 6 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:1155282 CAPLUS

DOCUMENT NUMBER: 143:427372

TITLE: Methods and compositions for preventing or treating periodontal diseases using, for example, Resolvin E1

INVENTOR(S): Van, Dyke Thomas E.; Petasis, Nicos A.; Serhan, Charles N.

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 19 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

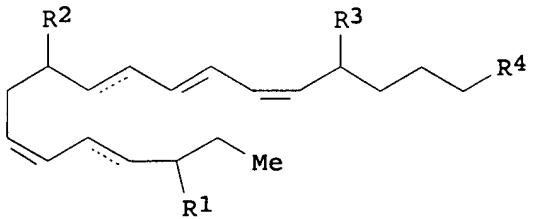
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| US 2005238589 | A1 | 20051027 | US 2005-106141 | 20050414 |
| WO 2005105025 | A1 | 20051110 | WO 2005-US12552 | 20050414 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KM, KP, KR, KZ,
LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA,
NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL,
SM, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA,
ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
MR, NE, SN, TD, TG | | | | |

PRIORITY APPLN. INFO.: US 2004-562099P P 20040414

OTHER SOURCE(S) : MARPAT 143:427372

GI



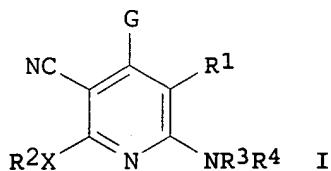
I

AB Methods and compns. for preventing or treating periodontal diseases, including gingivitis and periodontitis are provided. The compns. comprise a prophylactically or therapeutically effective amount of a compound I (R₁, R₂, R₃ = OR, OX₁, SR, SX₂, N(R)₂, NHX₃, NRC(O)R, NRC(O)N(R)₂, CO₂R, C(O)N(R)₂, SO₂R, NRSO₂, C(O)R, SO₂N(R)₂; R = C₁-6 aliphatic, 3-8 membered saturated, aryl; heterocycle, heteroaryl; X₁, X₂, X₃ = protecting group; R₄ = NRC(O)R, NRC(O)N(R), C(O)OR, C(O)N(R)₂, SO₂R, NRSO₂R, C(O)R, or SO₂N(R)₂), or a pharmaceutically acceptable salt or prodrug thereof and a pharmaceutically acceptable carrier. The composition further includes a COX-2 inhibitor selected from celecoxib, rofecoxib, and valdecoxib. The invention also provides methods for preventing or treating secondary diseases within or beyond the oral cavity that are related to periodontal disease, such as cardiovascular diseases, pregnancy complications, and diabetes. Thus, topical delivery of Resolvin E1 suspended in ethanol (7 µg/mL) every other day for 6 wk prevented both the bone loss and inflammatory changes in rabbits treated either with ligature alone or ligature plus topical Porphyromonas gingivalis (model of periodontal disease).

L8 ANSWER 7 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:824492 CAPLUS
 DOCUMENT NUMBER: 143:222525
 TITLE: Method of using 3-cyano-4-arylpypyridine derivatives as modulators of androgen receptor function, preparation thereof, and use with other agents
 INVENTOR(S): Nirschl, Alexandra A.; Hamann, Lawrence G.
 PATENT ASSIGNEE(S): USA
 SOURCE: U.S. Pat. Appl. Publ., 25 pp.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|----------------------------|----------|-----------------|----------|
| ----- | ----- | ----- | ----- | ----- |
| US 2005182105 | A1 | 20050818 | US 2005-48437 | 20050201 |
| PRIORITY APPLN. INFO.: | US 2004-541780P P 20040204 | | | |
| OTHER SOURCE(S): | MARPAT 143:222525 | | | |
| GI | | | | |



AB A method is provided for treating androgen receptor-associated conditions, such as age-related diseases, e.g. sarcopenia, employing a compound I [R1 = CN, H; X = O, S; R2 = (substituted) alkyl, (substituted) cycloalkyl, etc.; R3, R4 = H, (substituted) alkyl, etc.; G = (substituted) aryl, (substituted) heteroaryl], or a pharmaceutically acceptable salt or prodrug ester thereof. Preparation of selected I is described. I may be used in combination with other agents.

L8 ANSWER 8 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:696865 CAPLUS

DOCUMENT NUMBER: 143:193802

TITLE: Preparation of nitric oxide releasing prodrugs of diaryl-2(5H)-furanones as cyclooxygenase-2 inhibitors

Berthelette, Carl; Li, Lianhai; Beaulieu, Christian; Wang, Zhaoyin; Sturino, Claudio F.

PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.

SOURCE: PCT Int. Appl., 41 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| WO 2005070874 | A1 | 20050804 | WO 2005-CA84 | 20050125 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IS, IT, LT, LU, MC, NL, PL, PT,
RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML,
MR, NE, SN, TD, TG | | | | |

PRIORITY APPLN. INFO.: US 2004-540101P P 20040127

OTHER SOURCE(S): MARPAT 143:193802

GI

* STRUCTURE DIAGRAM TOO LARGE FOR DISPLAY - AVAILABLE VIA OFFLINE PRINT *

AB Title compds. I [n = 1-6; R1 = SO₂CH₃, SO₂NH₂; R2-3 = H, halo, alkoxy, etc.; R4 = alkyl, Ph, etc.] are prepared For instance, II is prepared in several steps from 4-(4-(methanesulfonyl)phenyl)-3-phenyl-5H-furan-2-one and hex-5-en-1-ol. I are nitric oxide-releasing prodrugs of

diaryl-2(5H)-furanones useful in the treatment of cyclooxygenase-2 mediated diseases [no data]. I may also be used as a combination therapy with low-dose aspirin to treat chronic cyclooxygenase-2 mediated diseases or conditions while also reducing the risk of thrombotic cardiovascular events.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 9 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:460617 CAPLUS
DOCUMENT NUMBER: 144:186912
TITLE: Examination of 209 drugs for inhibition of cytochrome P450 2C8
AUTHOR(S): Walsky, Robert L.; Gaman, Emily A.; Obach, R. Scott
CORPORATE SOURCE: Pharmacokinetics, Pharmacodynamics, and Drug Metabolism, Pfizer Global Research and Development, Groton/New London Laboratories, Groton, CT, USA
SOURCE: Journal of Clinical Pharmacology (2005), 45(1), 68-78
CODEN: JCPCBR; ISSN: 0091-2700
PUBLISHER: Sage Publications
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Cytochrome P 450 2C8 is involved in the metabolism of drugs such as paclitaxel, repaglinide, rosiglitazone, and cerivastatin, among others. An in vitro assessment of 209 frequently prescribed drugs and related xenobiotics was carried out to examine their potential to inhibit CYP2C8. A validated sensitive, moderate-throughput high-performance liquid chromatog./tandem mass spectrometry(HPLC/MS/MS) assay was used to detect N-desethylamodiaquine, the CYP2C8-derived major metabolite of amodiaquine metabolism, using heterologously expressed recombinant CYP2C8 (rhCYP2C8) and pooled human liver microsomes. The 209 drugs were first tested at 30 μ M for their ability to inhibit rhCYP2C8. Forty-eight compds. exhibited greater than 50% inhibition and were further evaluated for measurement of IC₅₀. The six most potent inhibitors (IC₅₀ < 1 μ M) from this set were measured for IC₅₀ in pooled human liver microsomes, and the most potent inhibitor identified was the leukotriene receptor antagonist, montelukast (IC₅₀ = 19.6 nM). Inhibitors of CYP2C8 were identified from a wide variety of therapeutic classes, with no single class predominating. Other potent inhibitors included candesartan cilexetil (cyclohexylcarbonate ester prodrug of candesartan), zafirlukast, clotrimazole, felodipine, and mometasone furoate. Seventeen moderate inhibitors of rhCYP2C8 (1 < IC₅₀ < 10 μ M) included salmeterol, raloxifene, fenofibrate, ritonavir, levothyroxine, tamoxifen, loratadine, quercetin, oxybutynin, medroxyprogesterone, simvastatin, ketoconazole, ethinyl estradiol, spironolactone, lovastatin, nifedipine, and irbesartan. These in vitro data were used along with clin. pharmacokinetic information in predicting potential drug-drug interactions that could occur by inhibition of CYP2C8. Although almost all drugs tested are not expected to cause drug interactions via inhibition of CYP2C8, montelukast was identified as being of concern as a potential inhibitor of clin. relevance. These findings are discussed in context to potential drug interactions that could be observed between these agents and drugs for which CYP2C8 is involved in metabolism and warrant investigation of the possibility of clin. drug interactions mediated by inhibition of this enzyme.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 10 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:451140 CAPLUS
DOCUMENT NUMBER: 142:476264

TITLE: Compositions of a cyclooxygenase-2 selective inhibitor and a neurotrophic factor-modulating agent for the treatment of central nervous system-mediated disorders
INVENTOR(S): Taylor, Duncan P.; Stephenson, Diane T.
PATENT ASSIGNEE(S): Pharmacia & Upjohn Company LLC, USA
SOURCE: PCT Int. Appl., 153 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|----------|-----------------|------------|
| WO 2005046615 | A2 | 20050526 | WO 2004-US37882 | 20041112 |
| WO 2005046615 | A3 | 20060622 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, CN, CO, CR, CU, CZ, DE, DK, GE, GH, GM, HR, HU, ID, IL, LK, LR, LS, LT, LU, LV, MA, NO, NZ, OM, PG, PH, PL, PT, TJ, TM, TN, TR, TT, TZ, UA, RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, AZ, BY, KG, KZ, MD, RU, TJ, EE, ES, FI, FR, GB, GR, HU, IE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, NE, SN, TD, TG | BA, BB, BG, BR, BW, BY, BZ, CA, CH, EC, EE, EG, ES, FI, GB, GD, KG, KP, KR, KZ, LC, MN, MW, MX, MZ, NA, NI, SG, SK, SL, SY, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW, BE, BG, CH, CY, CZ, DE, DK, MC, NL, PL, PT, RO, GW, ML, MR, | | | |
| CA 2545731 | AA | 20050526 | CA 2004-2545731 | 20041112 |
| US 2005148589 | A1 | 20050707 | US 2004-987876 | 20041112 |
| EP 1684784 | A2 | 20060802 | EP 2004-801034 | 20041112 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK, HR, IS, YU | | | | |
| PRIORITY APPLN. INFO.: | | | US 2003-519471P | P 20031112 |
| | | | WO 2004-US37882 | W 20041112 |

OTHER SOURCE(S): MARPAT 142:476264
AB The invention provides compns. and methods for the treatment of central nervous system-mediated disorders. More particularly, the invention provides a combination therapy for the treatment of a central nervous system-mediated disorder which comprises the administration of a neurotrophic factor-modulating agent in combination with a cyclooxygenase-2 selective inhibitor.

L8 ANSWER 11 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2005:409223 CAPLUS
DOCUMENT NUMBER: 142:441891
TITLE: Method and compositions for the treatment and prevention of pain and inflammation with cyclooxygenase-2 inhibitors and polyunsaturated fatty acids
INVENTOR(S): Pulaski, Steven P.; Kundel, Susan
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: U.S. Pat. Appl. Publ., 61 pp., Cont.-in-part of U.S. Ser. No. 215,539.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 2
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|-------------|
| US 2005101563 | A1 | 20050512 | US 2004-783160 | 20040219 |
| US 2003114416 | A1 | 20030619 | US 2002-215539 | 20020809 |
| CN 1575182 | A | 20050202 | CN 2002-820121 | 20020813 |
| ZA 2004001163 | A | 20050622 | ZA 2004-1163 | 20040212 |
| PRIORITY APPLN. INFO.: | | | US 2001-312211P | P 20010814 |
| | | | US 2002-215539 | A2 20020809 |

AB A method of preventing or treating pain or inflammation in a subject is provided by administering to the subject a Cox-2 inhibitor and a polyunsatd. fatty acid, or a prodrug thereof, wherein the amount of a Cox-2 inhibitor and polyunsatd. fatty acid or a pharmaceutically acceptable salt or prodrug thereof together constitute a pain or inflammation suppressing treatment or prevention effective amount. Glucosamine and/or chondroitin can optionally be present. Therapeutic compns. that contain the combination of Cox-2 inhibitor and polyunsatd. fatty acid and, optionally, the glucosamine and/or chondroitin, are disclosed, as are pharmaceutical compns.

L8 ANSWER 12 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:259661 CAPLUS

DOCUMENT NUMBER: 142:336520

TITLE: Preparation, pharmaceutical compositions, and methods comprising combinations of 2-alkylidene-19-nor-vitamin D derivatives and a cyclooxygenase-2 inhibitor

INVENTOR(S): Thompson, David D.

PATENT ASSIGNEE(S): Pfizer Inc., USA

SOURCE: U.S. Pat. Appl. Publ., 20 pp.

CODEN: USXXCO

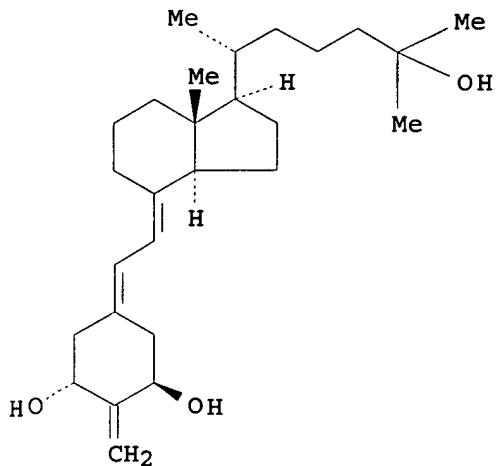
DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|------------|
| US 2005065130 | A1 | 20050324 | US 2004-943561 | 20040916 |
| WO 2005027918 | A1 | 20050331 | WO 2004-IB2913 | 20040906 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG | | | | |
| PRIORITY APPLN. INFO.: | | | US 2003-504003P | P 20030919 |
| GI | | | | |



AB The invention relates to pharmaceutical compns., and methods of treatment comprising administering to a patient in need of a combination of a 2-alkyldene-19-nor-vitamin D derivative and a cyclooxygenase-2 inhibitor, or a pharmaceutically acceptable salt or prodrug thereof. Particularly, the invention relates to pharmaceutical compns. and methods of treatment comprising administering to a patient in need of 2-methylene-19-nor-20(S)-10,25-dihydroxyvitamin D₃ and a cyclooxygenase-2 inhibitor, or a pharmaceutically acceptable salt or prodrug thereof. Thus, 1 α ,25-dihydroxy-2-methylene-19-norvitamin D₃ (I) was prepared in 11 steps from (-)-quinic acid. and (20S)-1 α ,25-dihydroxy-2-methylene-19-norvitamine D₃ was prepared from (20S)-25-[(triethylsilyl)oxy]-des-A,B-cholestan-8-one in 4 steps.

L8 ANSWER 13 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:216610 CAPLUS

DOCUMENT NUMBER: 142:291412

TITLE: Compositions of a cyclooxygenase-2 selective inhibitor and a corticotropin releasing factor antagonist for the treatment of ischemic-mediated central nervous system disorders or injury

INVENTOR(S): Arneric, Stephen P.

PATENT ASSIGNEE(S): Pharmacia Corporation, USA

SOURCE: PCT Int. Appl., 155 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| WO 2005020910 | A2 | 20050310 | WO 2004-US27600 | 20040826 |
| WO 2005020910 | A3 | 20050609 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |

RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG

US 2005085479 A1 20050421 US 2004-926751 20040826
PRIORITY APPLN. INFO.: US 2003-498148P P 20030827

OTHER SOURCE(S): MARPAT 142:291412

AB The invention provides compns. and methods for the treatment of ischemic-mediated central nervous system disorder or injury. More particularly, the invention provides a combination therapy for the treatment of a central nervous system ischemic-mediated disorder or injury comprising the administration to a subject of a cyclooxygenase-2 selective inhibitor and a corticotropin releasing factor antagonist or a pharmaceutically acceptable salt or a prodrug thereof.

L8 ANSWER 14 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:177827 CAPLUS

DOCUMENT NUMBER: 142:254634

TITLE: Compositions of a cyclooxygenase-2 selective inhibitor and a serotonin-modulating agent for the treatment of central nervous system damage

INVENTOR(S): Stephenson, Diane T.

PATENT ASSIGNEE(S): Pharmacia Corporation, USA

SOURCE: PCT Int. Appl., 172 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 2005018541 | A2 | 20050303 | WO 2004-US22059 | 20040708 |
| WO 2005018541 | A3 | 20060309 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2005080084 | A1 | 20050414 | US 2004-887112 | 20040708 |
| PRIORITY APPLN. INFO.: | | | US 2003-486549P | P 20030711 |

OTHER SOURCE(S): MARPAT 142:254634

AB The invention provides compns. and methods for the treatment of central nervous system damage in a subject. More particularly, the invention provides a combination therapy for the treatment of a central nervous system ischemic condition or a central nervous system traumatic injury comprising the administration to a subject of a serotonin-modulating agent in combination with a cyclooxygenase-2 selective inhibitor.

L8 ANSWER 15 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:99157 CAPLUS

DOCUMENT NUMBER: 142:170033

TITLE: Methods and compositions for the treatment or

prevention of human immunodeficiency virus and related conditions using cyclooxygenase-2 selective inhibitors and antiviral agents

INVENTOR(S) : Maziasz, Timothy
 PATENT ASSIGNEE(S) : USA
 SOURCE : U.S. Pat. Appl. Publ., 172 pp.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|------------|
| US 2005026902 | A1 | 20050203 | US 2004-769485 | 20040130 |
| PRIORITY APPLN. INFO.: | | | US 2003-443910P | P 20030131 |

OTHER SOURCE(S) : MARPAT 142:170033
 AB The present invention provides compns. and methods for the treatment of human immunodeficiency virus (HIV) infection as well as HIV associated diseases and related disorders. More particularly, the invention provides a combination therapy for the treatment of HIV infection as well as HIV associated diseases and related disorders comprising the administration to a subject of an anti-human immunodeficiency virus agent in combination with a cyclooxygenase-2 selective inhibitor or an isomer or a pharmaceutically acceptable salt, ester, or prodrug thereof.

L8 ANSWER 16 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2005:76247 CAPLUS
 DOCUMENT NUMBER: 142:148812
 TITLE: Compositions of a cyclooxygenase-2 selective inhibitor and a non-NMDA glutamate modulator for the treatment of central nervous system damage
 INVENTOR(S) : Stephenson, Diane T.; Taylor, Duncan P.
 PATENT ASSIGNEE(S) : Pharmacia Corporation, USA
 SOURCE: PCT Int. Appl., 150 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|------------|
| WO 2005007106 | A2 | 20050127 | WO 2004-US22189 | 20040708 |
| WO 2005007106 | A3 | 20060608 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI,
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: BW, GH, GM, KE, LS, MW, MZ, NA, SD, SL, SZ, TZ, UG, ZM, ZW, AM,
AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK,
EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE,
SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE,
SN, TD, TG | | | | |
| US 2005101597 | A1 | 20050512 | US 2004-887035 | 20040708 |
| PRIORITY APPLN. INFO.: | | | US 2003-486654P | P 20030710 |

OTHER SOURCE(S) : MARPAT 142:148812
 AB The invention provides compns. and methods for the treatment of central

nervous system damage in a subject. More particularly, the invention provides a combination therapy for the treatment of a central nervous system ischemic condition or a central nervous system traumatic injury comprising the administration to a subject of a non-NMDA glutamate modulator in combination with a cyclooxygenase-2 selective inhibitor.

L8 ANSWER 17 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:1020415 CAPLUS
DOCUMENT NUMBER: 142:190038
TITLE: Selective cyclooxygenase-2 inhibitors: similarities and differences
AUTHOR(S): Brune, K.; Hinz, B.
CORPORATE SOURCE: Department of Experimental and Clinical Pharmacology and Toxicology, Emil Fischer Center, Friedrich Alexander University, Erlangen, Germany
SOURCE: Scandinavian Journal of Rheumatology (2004), 33(1), 1-6
CODEN: SJRHAT; ISSN: 0300-9742
PUBLISHER: Taylor & Francis
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English

AB A review. The enzyme cyclooxygenase (COX) was shown to exist as two distinct isoforms about a decade ago. COX-1 is constitutively expressed as a 'housekeeping' enzyme in nearly all tissues, and mediates physiol. responses (e.g. cytoprotection of the stomach, and platelet aggregation). On the other hand, COX-2, expressed by cells involved in inflammation (e.g. macrophages, monocytes, synoviocytes), has emerged as the isoform that is primarily responsible for the synthesis of prostanoids involved in acute and chronic inflammatory states. Consequently, the hypothesis that selective inhibition of COX-2 might have therapeutic actions similar to those of non-steroidal anti-inflammatory drugs, but without causing gastrointestinal side effects, was the rationale for the development of selective inhibitors of the COX-2 isoenzyme. Selective COX-2 inhibitors currently used in the clinic are the sulfonamides celecoxib and valdecoxib (parecoxib is a prodrug of valdecoxib), as well as the methylsulfones rofecoxib and etoricoxib. Furthermore, the phenylacetic acid derivative lumiracoxib has gained permission recently to be marketed in Europe. This review discusses the clin. relevant similarities and differences of these substances, with particular emphasis on their diverse pharmacokinetic characteristics.

REFERENCE COUNT: 47 THERE ARE 47 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 18 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:754407 CAPLUS
DOCUMENT NUMBER: 141:271579
TITLE: Treatment and prevention of obesity with COX-2 inhibitors alone or in combination with weight-loss agents
INVENTOR(S): Briggs, Michael; Ornberg, Richard; Hauser, Scott; Koki, Alane
PATENT ASSIGNEE(S): Pharmacia Corporation, USA
SOURCE: PCT Int. Appl., 180 pp.
CODEN: PIXXD2
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|------|-----------------|------|
|------------|------|------|-----------------|------|

| | | | | |
|---------------|---|----------|----------------|----------|
| WO 2004078113 | A2 | 20040916 | WO 2004-US3219 | 20040205 |
| WO 2004078113 | A3 | 20051013 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI | | | |
| RW: | BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU,
MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN,
GQ, GW, ML, MR, NE, SN, TD, TG | | | |

| | | | | |
|---------------|----|----------|----------------|----------|
| US 2004204472 | A1 | 20041014 | US 2004-773019 | 20040205 |
|---------------|----|----------|----------------|----------|

| | | | | |
|------------------------|--|-----------------|---|----------|
| PRIORITY APPLN. INFO.: | | US 2003-451885P | P | 20030304 |
|------------------------|--|-----------------|---|----------|

AB A method for preventing or treating obesity and obesity-related complications in a subject involves a monotherapy with a Cox-2 inhibitor or a combination therapy with a Cox-2 inhibitor and a conventional weight-loss agent. Also described are therapeutic compns. comprising a Cox-2 inhibitor and a conventional weight-loss agent. Pharmaceutical compns. and kits for implementing the present method are also described.

L8 ANSWER 19 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:739958 CAPLUS

DOCUMENT NUMBER: 141:260542

TITLE: Preparation of nitric oxide releasing prodrugs of diaryl-2-(5H)-furanones as selective cyclooxygenase-2 inhibitors

INVENTOR(S): Berthelette, Carl; Li, Lianhai; Sturino, Claudio;
Wang, Zhaoxin

PATENT ASSIGNEE(S): Can.

SOURCE: U.S. Pat. Appl. Publ., 19 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

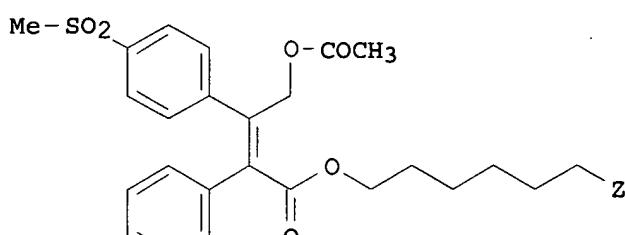
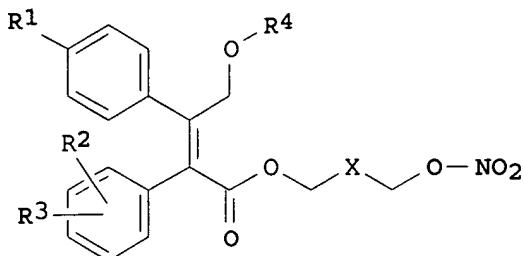
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|-----------------|-----------------|----------|
| US 2004176331 | A1 | 20040909 | US 2004-790288 | 20040301 |
| AU 2004240700 | A1 | 20041202 | AU 2004-240700 | 20040301 |
| CA 2517490 | AA | 20041202 | CA 2004-2517490 | 20040301 |
| WO 2004103955 | A1 | 20041202 | WO 2004-CA314 | 20040301 |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NA, NI
NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY,
TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE,
BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PL, PT, RO, SE, SI,
SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN,
TD, TG | | | |
| EP 1601644 | A1 | 20051207 | EP 2004-761562 | 20040301 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, PL, SK | | | |
| PRIORITY APPLN. INFO.: | | US 2003-452124P | P | 20030305 |
| | | WO 2004-CA314 | W | 20040301 |

OTHER SOURCE(S): MARPAT 141:260542

GI



AB Title compds. I [X = (CH₂)_n; n = 3-6; R1 = SO₂Me, SO₂NH₂, SO₂NHCOCF₃, etc.; R2, R3 = H, halo, alkoxy, etc.; R4 = CO-alkyl, CO(CH₂)_mR₅R₆; m = 1-4; R5, R6 = H, halo-substituted alkyl] and their pharmaceutically acceptable salts were prepared. For example, O-alkylation of AgNO₃ by bromide II (Z = Br), e.g., prepared from Rofecoxib in 6-steps, afforded nitrooxyhexyl II (Z = -ONO₂). In human blood PGE₂ inhibition production assays, nitrooxyhexyl II (Z = -ONO₂) exhibited an IC₅₀ value of 0.22 μM. Of note, the "unconverted prodrugs" of compds. I are inactive inhibitors of COX-1 and COX-2 activity. Compds. I are claimed useful for the treatment of cyclooxygenase-2 mediated diseases or conditions.

L8 ANSWER 20 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:589414 CAPLUS

DOCUMENT NUMBER: 141:134107

TITLE: A method for the treatment, prevention, or inhibition of a CNS disorder and/or pain and inflammation using a combination of duloxetine, venlafaxine or atomoxetine and a cyclooxygenase-2 selective inhibitor and compositions thereof

INVENTOR(S): Arneric, Stephen P.

PATENT ASSIGNEE(S): Pharmacia Corporation, USA

SOURCE: PCT Int. Appl., 208 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---------------|------|----------|-----------------|----------|
| WO 2004060366 | A1 | 20040722 | WO 2003-US38751 | 20031206 |

W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
 CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
 GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
 LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO,
 NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ,
 TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
 RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
 BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
 ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,
 TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG
 US 2004235925 A1 20041125 US 2003-727717 20031204
 CA 2508884 AA 20040722 CA 2003-2508884 20031206
 AU 2003294590 A1 20040729 AU 2003-294590 20031206
 BR 2003017361 A 20051116 BR 2003-17361 20031206
 PRIORITY APPLN. INFO.: US 2002-433790P P 20021217
 WO 2003-US38751 W 20031206

OTHER SOURCE(S): MARPAT 141:134107

AB A method of treating, preventing, or inhibiting a CNS disorder and/or pain and inflammation or an inflammation-associated disorder in a subject in need of such treatment or prevention provides for treating the subject with duloxetine, venlafaxine or atomoxetine and a cyclooxygenase-2 selective inhibitor or prodrug thereof, wherein the amount of duloxetine, venlafaxine or atomoxetine and the amount of a cyclooxygenase-2 selective inhibitor or prodrug thereof together constitute a CNS disorder, pain and inflammation, or inflammation-associated disorder suppressing treatment, prevention, or inhibition effective amount of the composition

Compns.

and pharmaceutical compns. that contain duloxetine, venlafaxine or atomoxetine and a cyclooxygenase-2 selective inhibitor are also disclosed.

L8 ANSWER 21 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:589409 CAPLUS

DOCUMENT NUMBER: 141:117197

TITLE: Compositions and a method for the treatment, prevention, or inhibition of a CNS disorder and/or pain and inflammation using a combination of reboxetine and a cyclooxygenase-2 selective inhibitor

INVENTOR(S): Arneric, Stephen P.

PATENT ASSIGNEE(S): Pharmacia Corporation, USA

SOURCE: PCT Int. Appl., 192 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 2004060361 | A2 | 20040722 | WO 2003-US38770 | 20031205 |
| WO 2004060361 | A3 | 20040902 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC,
LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO,
NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ,
TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW
RW: BW, GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE,
ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK,
TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |

| | | | | |
|--|----|----------|-----------------|------------|
| US 2004204411 | A1 | 20041014 | US 2003-727918 | 20031204 |
| CA 2510584 | AA | 20040722 | CA 2003-2510584 | 20031205 |
| AU 2003303625 | A1 | 20040729 | AU 2003-303625 | 20031205 |
| EP 1575594 | A2 | 20050921 | EP 2003-808444 | 20031205 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| BR 2003017511 | A | 20051116 | BR 2003-17511 | 20031205 |
| JP 2006513237 | T2 | 20060420 | JP 2004-565231 | 20031205 |
| PRIORITY APPLN. INFO.: | | | US 2002-433780P | P 20021217 |
| | | | WO 2003-US38770 | W 20031205 |

OTHER SOURCE(S): MARPAT 141:117197

AB A method of treating, preventing, or inhibiting a CNS disorder and/or pain and inflammation, or an inflammation-associated disorder in a subject in need of such treatment, prevention, or inhibition provides administering to the subject a combination of reboxetine and a cyclooxygenase-2 selective inhibitor or prodrug thereof. Pharmaceutical compns. containing reboxetine and a cyclooxygenase-2 selective inhibitor are also disclosed. For example, a combination of reboxetine and celebrex provided an effective anti-inflammatory activity in a rat carrageenan foot pad edema test, an effective analgesic activity in a rat carrageenan-induced analgesia test, and it was an efficacious treatment for collagen-induced arthritis in mice.

L8 ANSWER 22 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:412933 CAPLUS

DOCUMENT NUMBER: 140:423574

TITLE: Preparation of nitric oxide releasing prodrugs of diaryl-2-(5H)-furanones as cyclooxygenase-2 inhibitors

INVENTOR(S): Young, Robert N.; Wang, Zhaoyin

PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.

SOURCE: PCT Int. Appl., 65 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

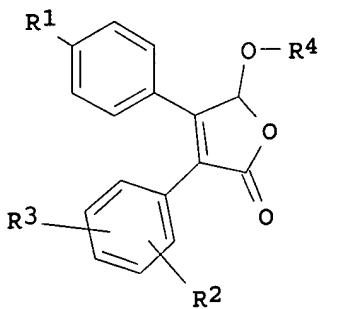
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|------------|
| WO 2004041803 | A1 | 20040521 | WO 2003-CA1691 | 20031103 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BW, BY, BZ, CA, CH,
CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, EG, ES, FI, GB, GD,
GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK,
LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ,
OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM,
TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2003283096 | A1 | 20040607 | AU 2003-283096 | 20031103 |
| PRIORITY APPLN. INFO.: | | | US 2002-423866P | P 20021105 |
| | | | WO 2003-CA1691 | W 20031103 |

OTHER SOURCE(S): MARPAT 140:423574

GI



AB The title compds. I [R1 = SO₂Me, etc.; R2, R3 = H, halo, etc.; R4 = NOM, etc.; m = 1 or 2] are prepared. The above compds. may be used as a combination therapy with low-dose aspirin to treat chronic cyclooxygenase-2 mediated diseases while simultaneously reducing the risk of thrombotic cardiovascular events.

L8 ANSWER 23 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:392439 CAPLUS

DOCUMENT NUMBER: 140:400095

TITLE: Stereoisomers of p-hydroxy-milnacipran, and therapeutic use

INVENTOR(S): Rariy, Roman V.; Heffernan, Michael; Buchwald, Stephen L.; Swager, Timothy M.

PATENT ASSIGNEE(S): Collegium Pharmaceutical, Inc., USA

SOURCE: PCT Int. Appl., 163 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 6

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 2004039320 | A2 | 20040513 | WO 2003-US33681 | 20031022 |
| WO 2004039320 | A3 | 20040624 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2503381 | AA | 20040513 | CA 2003-2503381 | 20031022 |
| AU 2003284342 | A1 | 20040525 | AU 2003-284342 | 20031022 |
| US 2004142904 | A1 | 20040722 | US 2003-691465 | 20031022 |
| US 7038085 | B2 | 20060502 | | |
| EP 1578719 | A2 | 20050928 | EP 2003-776524 | 20031022 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| JP 2006503920 | T2 | 20060202 | JP 2005-501895 | 20031022 |
| PRIORITY APPLN. INFO.: | | | US 2002-421640P | P 20021025 |
| | | | US 2002-423062P | P 20021101 |

US 2003-445142P P 20030205
 WO 2003-US33681 W 20031022

OTHER SOURCE(S): MARPAT 140:400095

AB The invention relates generally to the enantiomers of p-hydroxymilnacipran or congeners thereof. Biol. assays revealed that racemic p-hydroxymilnacipran is approx. equipotent in inhibiting serotonin and norepinephrine uptake ($IC_{50} = 28.6$ nM for norepinephrine, $IC_{50} = 21.7$ nM for serotonin). Interestingly, (+)-p-hydroxymilnacipran is a more potent inhibitor of norepinephrine uptake than serotonin uptake ($IC_{50} = 10.3$ nM for norepinephrine, $IC_{50} = 22$ nM for serotonin). In contrast, (-)-p-hydroxymilnacipran is a more potent inhibitor of serotonin uptake compared to norepinephrine uptake ($IC_{50} = 88.5$ nM for norepinephrine, $IC_{50} = 40.3$ nM for serotonin). The invention also relates to salts and prodrug forms of the above compds. In certain embodiments, the compds. of the invention and a pharmaceutically acceptable excipient are combined to prepare a formulation for administration to a patient. Finally, the invention relates to methods of treating mammals suffering from various afflictions, e.g., depression, chronic pain, or fibromyalgia, comprising administering to a mammal in need thereof a therapeutically effective amount of a compound of the invention. Compound preparation is included.

L8 ANSWER 24 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:101124 CAPLUS

DOCUMENT NUMBER: 140:163574

TITLE: Preparation of nitric oxide releasing diaryl-2-(5H)-furanone prodrugs as selective cyclooxygenase-2 inhibitors for treatment inflammatory diseases

INVENTOR(S): Berthelette, Carl; Lachance, Nicholas; Li, Lianhai; Sturino, Claudio; Wang, Zhaoyin; Young, Robert N.; Dufresne, Claude

PATENT ASSIGNEE(S): Merck Frosst Canada & Co., Can.

SOURCE: PCT Int. Appl., 129 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

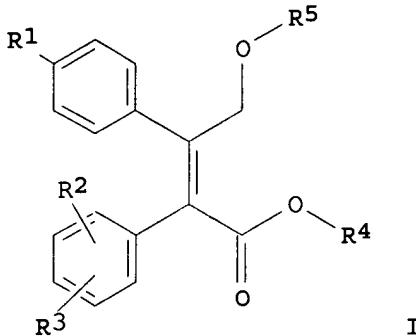
FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 2004011421 | A1 | 20040205 | WO 2003-CA1115 | 20030724 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2493082 | AA | 20040205 | CA 2003-2493082 | 20030724 |
| AU 2003252515 | A1 | 20040216 | AU 2003-252515 | 20030724 |
| EP 1527045 | A1 | 20050504 | EP 2003-771010 | 20030724 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| US 2005261245 | A1 | 20051124 | US 2005-521075 | 20050112 |
| PRIORITY APPLN. INFO.: | | | US 2002-398683P | P 20020726 |

US 2002-435341P
WO 2003-CA1115P 20021220
W 20030724OTHER SOURCE(S) :
GI

MARPAT 140:163574



AB Title compds. I [R1 = S(O)2CH3, S(O)2NH2, S(O)2NHC(=O)CF3, etc.; R2, R3 = H, halo, alkoxy, etc.; R4 = H, (un)substituted alkyl, e.g., halo, Ph, naphthyl, etc.; R5 = NOx, C(=O)-E-alkyl-W-NOx, C(=O)-E-alkyl-Ar-alkyl-W-NOx; x = 1, 2; E = bond, O, S, etc.; W = O, S, C[CO2Rb]2; Ar = (un)substituted Ph, naphthyl, HET3; HET3 = benzimidazolyl, benzofuranyl, benzopyrazolyl, etc.; Rb = (un)substituted alkyl, Ph, naphthyl, etc.] and their pharmaceutically acceptable salts were prepared. For example, allylic bromination of Me (2E)-3-[4-(methylsulfonyl)phenyl]-2-phenylbut-2-enoate, e.g., prepared from 1-(4-methanesulfonylphenyl)ethanone in 2 steps, followed by O-alkylation of AgNO3 afforded nitrate ester I [R1 = 4-S(O)2CH3; R2, R3 = H; R4 = CH3; R5 = NO2] in 23% overall yield. In human whole blood LPS induced PGE2 and TXB2 production assays, compds. I have a COX-2 potency and COX-2/COX-1 selectivity comparable to rofecoxib. In paw edema assays in rat, compound I [R1 = 4-S(O)2CH3; R2, R3 = H; R4 = CH3; R5 = CO2(CH2)4ONO2] exhibited 42-79% inhibition of pain at 1-30 mg/kg dosage. Of note, compds. I are prodrugs of rofecoxib analogs and are claimed useful for the treatment of chronic COX-2 mediated diseases, while reducing the risk of thrombotic cardiovascular events. Compds. I are useful for treatments of osteoarthritis, rheumatoid arthritis, and chronic pain.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 25 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:20448 CAPLUS

DOCUMENT NUMBER: 140:87676

TITLE: Derivatives of gambogic acid and analogs as activators of caspases and inducers of apoptosis

INVENTOR(S): Tseng, Ben; Sirisoma, Nilantha Sudath; Cai, Sui Xiong; Zhang, Han-Zhong; Kasibhatla, Shailaja; Ollis, Kristin P.; Drewe, John A.

PATENT ASSIGNEE(S): Cytovia, Inc., USA

SOURCE: PCT Int. Appl., 92 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 2004002428 | A2 | 20040108 | WO 2003-US20668 | 20030701 |
| WO 2004002428 | A3 | 20050616 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, SY, TJ, TM, TN, TR, TT, TZ, UA, UG, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2491698 | AA | 20040108 | CA 2003-2491698 | 20030701 |
| AU 2003267977 | A1 | 20040119 | AU 2003-267977 | 20030701 |
| US 2004082066 | A1 | 20040429 | US 2003-609670 | 20030701 |
| EP 1562598 | A2 | 20050817 | EP 2003-748924 | 20030701 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| CN 1738620 | A | 20060222 | CN 2003-815628 | 20030701 |
| JP 2006507227 | T2 | 20060302 | JP 2004-518157 | 20030701 |
| PRIORITY APPLN. INFO.: | | | US 2002-392358P | P 20020701 |
| | | | US 2002-413649P | P 20020926 |
| | | | WO 2003-US20668 | W 20030701 |

OTHER SOURCE(S): MARPAT 140:87676

AB The invention is directed to derivs. of gambogic acid and analogs thereof. Exemplary gambogic acid derivs. of the present invention include, among others, derivs. substituted in the C10 and C28 positions of gambogic acid. The present invention also relates to the discovery that certain preferred compds. of the invention are activators of caspases and inducers of apoptosis. Therefore, the activators of caspases and inducers of apoptosis of this invention can be used to induce cell death in a variety of clin. conditions in which uncontrolled growth and spread of abnormal cells occurs.

L8 ANSWER 26 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2004:2830 CAPLUS

DOCUMENT NUMBER: 140:59410

TITLE: Preparation of nitrooxy derivatives of cyclooxygenase-2 inhibitors

INVENTOR(S): Del Soldato, Piero; Santus, Giancarlo

PATENT ASSIGNEE(S): Nicox S.A., Fr.

SOURCE: PCT Int. Appl., 27 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| WO 2004000781 | A2 | 20031231 | WO 2003-EP6502 | 20030620 |
| WO 2004000781 | A3 | 20041014 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, | | | | |

| | | | | |
|---|----|----------|-----------------|----------|
| PG, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR,
TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2491209 | AA | 20031231 | CA 2003-2491209 | 20030620 |
| AU 2003245972 | A1 | 20040106 | AU 2003-245972 | 20030620 |
| EP 1517889 | A2 | 20050330 | EP 2003-738069 | 20030620 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| CN 1662490 | A | 20050831 | CN 2003-814682 | 20030620 |
| JP 2005530836 | T2 | 20051013 | JP 2004-514803 | 20030620 |
| ZA 2004010060 | A | 20051020 | ZA 2004-10060 | 20041213 |
| NO 2005000346 | A | 20050228 | NO 2005-346 | 20050121 |
| US 2006106082 | A1 | 20060518 | US 2005-516938 | 20050913 |
| PRIORITY APPLN. INFO.: IT 2002-MI1391 A 20020625 | | | | |
| WO 2003-EP6502 W 20030620 | | | | |

OTHER SOURCE(S): MARPAT 140:59410

AB Disclosed are new compds. able to release COX-2 inhibitors and NO (no data) having formula M-T-YA-NO₂ [wherein M-T = the residue of a COX-2 selective inhibitor (T = SO₂NH, SO₂NR, CO, O, S, NH, N(SO₂R); R = C₁-10 alkyl; the COX-2 selective inhibitor, M-TH or M-TOH, has to meet test 2 mentioned in the description); YA = -(B)b₀-(C)c₀- [b₀, c₀ = 0, 1, with the proviso that b₀ and c₀ cannot be simultaneously 0; B = TB-X₂-TB₁; TB = CO, X; X = O, S, NH, NR, R (defined above); TB = CO when T = SO₂NH, SO₂NR-O, S, NH, or N(SO₂R), TB = X when T = CO; TB₁ = CO or X (defined above); X₂ = a divalent radical selected from the following compds. Q or Q₁, etc. (n₁, n₂ = 0, 1; R₂, R₃ = H, Me; Y₁ = CH₂CH₂, CH:CH(CH₂)n₂; n₂ = 0, 1)]] for the treatment and/or prophylaxis of inflammatory disorders, pain, fever, cardiovascular disease, gastrointestinal disorders, tumors, Alzheimer's disease, or disorders resulting from elevated levels of COX-2. These compds. including 5-niroxypentanoc acid, 4-nitrooxybutyric acid, and 4-nitrooxybutyramide, 2-nitroxymethylbenzoic acid ester derivs. mitigate or remove the known side-effects of COX-2 inhibitors. The inflammatory disorders are selected from the group consisting of, but not limited to, arthritis, rheumatoid arthritis, osteoarthritis, allergic rhinitis, sinusitis, chronic obstructive pulmonary diseases, dermatitis, psoriasis, cystic fibrosis, multiple sclerosis, vasculitis and organ transplant rejection. The cardiovascular diseases are selected from the group consisting of, but not limited to, atherosclerosis, restenosis, coronary artery disease, angina, diabetes mellitus, diabetic nephropathy, diabetic retinopathy, stroke and myocardial infarct. The gastrointestinal disorders are selected from the group consisting of, but not limited to, inflammatory intestinal disorders, Crohn's disease, gastritis, ulcerative colitis, peptic ulcer, hemorrhagic ulcer, gastric hyperacidity, dyspepsia, gastroparesis, Zollinger-Ellison's syndrome, bacterial infections, hypersecretory states associated with systemic mastocytosis or basophilic leukemia and hyperhystaminemia. The disorders resulting from elevated levels of COX-2 are selected from the group consisting of, but not limited to, angiogenesis, arthritis, asthma, bronchitis, menstrual cramps, tendonitis, bursitis, neoplasia, ophthalmic diseases, pulmonary inflammations, central nervous system disorders, allergic rhinitis, atherosclerosis, endothelial disorders, organs and tissues preservation, inhibition and/or prevention of platelets aggregation. Thus, N-[6-[(2,4-difluorophenyl)thio]-2,3-dihydro-1-oxo-1-inden-5-yl]-N-[4-(chloro)butyroyloxymethyl]methanesulfonamide. A solution of chloromethyl (4-chloro)butyrate (1 g, 5.40 mmol) in anhydrous THF (5 mL) was slowly added dropwise in a suspension of N-[6-[(2,4-difluorophenyl)thio]-2,3-dihydro-1-oxo-1-inden-5-yl]methanesulfonamide sodium salt (2.04 g, 5.40 mmol) in

anhydrous THF (25 mL) and stirred at room temperature overnight to give, after workup and silica gel chromatog., N-[6-[(2,4-difluorophenyl)thio]-2,3-dihydro-1-oxo-1-inden-5-yl]-N-[4-(chloro)butyroyloxymethyl]methanesulfonamide (I). A solution of I (1 g, 1.98 mmol) in MeCN (20 mL) was added with AgNO₃ (0.67 g, 3.96 mmol), heated at 80° for 15 h in the absence of light, filtered to remove the silver salt, evaporated under vacuum, and purified by chromatog. on a silica gel column to give with n-hexane/ethyl acetate 8/2 as eluent to give 503 mg N-[6-[(2,4-difluorophenyl)thio]-2,3-dihydro-1-oxo-1-inden-5-yl]-N-[4-(nitrooxy)butyroyloxymethyl]methanesulfon amide.

L8 ANSWER 27 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:971878 CAPLUS

DOCUMENT NUMBER: 140:13075

TITLE: Monotherapy for the treatment of amyotrophic lateral sclerosis with cyclooxygenase-2 (COX 2) inhibitor(s)

INVENTOR(S): Isakson, Peter C.

PATENT ASSIGNEE(S): Pharmacia Corporation, USA

SOURCE: PCT Int. Appl., 182 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 2003101441 | A1 | 20031211 | WO 2003-US14548 | 20030528 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2004063752 | A1 | 20040401 | US 2003-444072 | 20030523 |
| CA 2487923 | AA | 20031211 | CA 2003-2487923 | 20030528 |
| AU 2003232096 | A1 | 20031219 | AU 2003-232096 | 20030528 |
| BR 2003011518 | A | 20050222 | BR 2003-11518 | 20030528 |
| EP 1509217 | A1 | 20050302 | EP 2003-756170 | 20030528 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| CN 1658853 | A | 20050824 | CN 2003-812637 | 20030528 |
| JP 2005531592 | T2 | 20051020 | JP 2004-508799 | 20030528 |
| PRIORITY APPLN. INFO.: | | | US 2002-384139P | P 20020531 |
| | | | US 2003-444072 | A 20030523 |
| | | | WO 2003-US14548 | W 20030528 |

OTHER SOURCE(S): MARPAT 140:13075

AB A method of treating, preventing, or inhibiting amyotrophic lateral sclerosis (ALS), in a subject in need of such treatment, inhibition or prevention. The method comprises administering to a subject one or more cyclooxygenase-2 selective inhibitor(s), or isomer(s), or pharmaceutically acceptable salt(s), ester(s), or prodrug(s) thereof, wherein the amount of the cyclooxygenase-2 selective inhibitor(s), isomer(s), ester(s), salt(s) or prodrug(s) thereof constitutes an ALS treatment, inhibition or prevention effective amount of the COX 2 inhibitor(s).

REFERENCE COUNT: 1 THERE ARE 1 CITED REFERENCES AVAILABLE FOR THIS

RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 28 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2003:971836 CAPLUS
 DOCUMENT NUMBER: 140:23256
 TITLE: Combination therapy for treatment of amyotrophic lateral sclerosis (ALS) with cyclooxygenase-2 (COX 2) inhibitor(s) and a second drug
 INVENTOR(S): Isakson, Peter C.
 PATENT ASSIGNEE(S): Pharmacia Corporation, USA
 SOURCE: PCT Int. Appl., 358 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 2003101380 | A2 | 20031211 | WO 2003-US14547 | 20030528 |
| WO 2003101380 | A3 | 20041111 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2004063751 | A1 | 20040401 | US 2003-444071 | 20030523 |
| CA 2487885 | AA | 20031211 | CA 2003-2487885 | 20030528 |
| AU 2003241400 | A1 | 20031219 | AU 2003-241400 | 20030528 |
| BR 2003011524 | A | 20050510 | BR 2003-11524 | 20030528 |
| EP 1539169 | A2 | 20050615 | EP 2003-731134 | 20030528 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| JP 2005534642 | T2 | 20051117 | JP 2004-508738 | 20030528 |
| PRIORITY APPLN. INFO.: | | | US 2002-384104P | P 20020531 |
| | | | US 2003-444071 | A 20030523 |
| | | | WO 2003-US14547 | W 20030528 |

OTHER SOURCE(S): MARPAT 140:23256
 AB A method of treating, preventing, or inhibiting ALS, in a subject in need of such treatment, inhibition or prevention. The method comprises administering to a subject one or more cyclooxygenase-2 selective inhibitor(s) or isomer(s) or pharmaceutically acceptable salt(s), ester(s), or prodrug(s) thereof, in combination with one or more second drugs, wherein the amount of the cyclooxygenase-2 selective inhibitor(s) or isomer(s) or pharmaceutically acceptable salt(s), ester(s), or prodrug(s) thereof in combination with the amount of second drug(s) constitutes an ALS treatment, inhibition or prevention effective amount

L8 ANSWER 29 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2003:855795 CAPLUS
 DOCUMENT NUMBER: 139:345939
 TITLE: Monotherapy for the treatment of Parkinson's disease with cyclooxygenase 2 (COX2) inhibitor(s)
 INVENTOR(S): Stephenson, Diane T.; Isakson, Peter C.; Maziasz,

PATENT ASSIGNEE(S) : Timothy J.
 SOURCE : Pharmacia Corporation, USA
 PCT Int. Appl., 186 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE : Patent
 LANGUAGE : English
 FAMILY ACC. NUM. COUNT : 1
 PATENT INFORMATION :

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 2003088959 | A2 | 20031030 | WO 2003-US11517 | 20030414 |
| WO 2003088959 | A3 | 20031231 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2482510 | AA | 20031030 | CA 2003-2482510 | 20030414 |
| AU 2003226379 | A1 | 20031103 | AU 2003-226379 | 20030414 |
| US 2004006100 | A1 | 20040108 | US 2003-412970 | 20030414 |
| BR 2003009337 | A | 20050215 | BR 2003-9337 | 20030414 |
| EP 1505962 | A2 | 20050216 | EP 2003-746984 | 20030414 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| JP 2005532293 | T2 | 20051027 | JP 2003-585711 | 20030414 |
| PRIORITY APPLN. INFO.: | | | US 2002-373317P | P 20020418 |
| | | | WO 2003-US11517 | W 20030414 |

OTHER SOURCE(S) : MARPAT 139:345939
 AB The invention provides a method for treating, preventing, or inhibiting Parkinson's disease (PD), in a subject in need of such treatment, inhibition or prevention. The method comprises treating the subject with one or more COX2 selective inhibitor(s), ester(s), salt(s) or prodrug(s) thereof, wherein the amount of the cyclooxygenase-2 selective inhibitor(s), ester(s), salt(s) or prodrug(s) thereof constitutes a PD treatment-, inhibition- or prevention-effective amount of the COX2 inhibitor(s).

L8 ANSWER 30 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2003:855794 CAPLUS
 DOCUMENT NUMBER: 139:345938
 TITLE: Combination therapy including cyclooxygenase 2 (COX2) inhibitor(s) for the treatment of Parkinson's disease
 INVENTOR(S) : Stephenson, Diane T.; Isakson, Peter C.; Maziasz, Timothy J.
 PATENT ASSIGNEE(S) : Pharmacia Corporation, USA
 SOURCE: PCT Int. Appl., 266 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE : Patent
 LANGUAGE : English
 FAMILY ACC. NUM. COUNT : 1
 PATENT INFORMATION :

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|-------|-------|-----------------|-------|
| ----- | ----- | ----- | ----- | ----- |

| | | | | |
|------------------------|--|----------|-----------------|------------|
| WO 2003088958 | A2 | 20031030 | WO 2003-US11269 | 20030414 |
| WO 2003088958 | A3 | 20040819 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| CA 2481934 | AA | 20031030 | CA 2003-2481934 | 20030414 |
| AU 2003223579 | A1 | 20031103 | AU 2003-223579 | 20030414 |
| US 2004034083 | A1 | 20040219 | US 2003-413348 | 20030414 |
| EP 1494664 | A2 | 20050112 | EP 2003-719717 | 20030414 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | |
| BR 2003009259 | A | 20050209 | BR 2003-9259 | 20030414 |
| JP 2005528403 | T2 | 20050922 | JP 2003-585710 | 20030414 |
| PRIORITY APPLN. INFO.: | | | US 2002-373311P | P 20020418 |
| | | | WO 2003-US11269 | W 20030414 |

OTHER SOURCE(S): MARPAT 139:345938

AB The invention discloses a method for treating, preventing, or inhibiting Parkinson's disease (PD) in a subject in need of such treatment, inhibition, or prevention. The method comprises treating the subject with one or more COX2 selective inhibitor(s) or isomer(s) or pharmaceutically acceptable salt(s), ester(s), or prodrug(s) thereof, in combination with one or more second drugs, wherein the amount of the COX2 selective inhibitor(s) or isomer(s) or pharmaceutically acceptable salt(s), ester(s), or prodrug(s) thereof in combination with the amount of second drug(s) constitutes a PD treatment-, inhibition- or prevention-effective amount

L8 ANSWER 31 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:656204 CAPLUS

DOCUMENT NUMBER: 139:191422

TITLE: Combinations of a cyclooxygenase-2 selective inhibitor and a TNF- α antagonist and therapeutic uses therefor

INVENTOR(S): Bennett, Dennis A.

PATENT ASSIGNEE(S): Pharmacia Corporation, USA

SOURCE: U.S. Pat. Appl. Publ., 39 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|-------|----------|-----------------|------------|
| ----- | ----- | ----- | ----- | ----- |
| US 2003157061 | A1 | 20030821 | US 2002-310454 | 20021205 |
| PRIORITY APPLN. INFO.: | | | US 2001-337802P | P 20011205 |

AB A method for the prevention, treatment, or inhibition of pain, inflammation, or inflammation-related disorder and for the prevention, treatment, or inhibition of a cardiovascular disease or disorder in a subject that is in need of such prevention, treatment or inhibition, involves the administration to the subject of a cyclooxygenase-2 selective inhibitor or prodrug thereof and a TNF- α antagonist. A method can also involve the treatment, prevention, or inhibition of cancer

in a subject in need of such treatment, prevention, or inhibition, by administering to the subject a cyclooxygenase-2 selective inhibitor or prodrug thereof and a TNF- α antagonist which is selected from the group consisting of a compound that affects the synthesis of TNF- α , a compound that inhibits the binding of TNF- α with a receptor specific for TNF- α , and a compound that interferes with intracellular signaling triggered by TNF- α binding with a receptor. Compns., pharmaceutical compns. and kits that can be used with the methods are also described.

L8 ANSWER 32 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:633408 CAPLUS

DOCUMENT NUMBER: 139:159977

TITLE: Treatment of colds and cough with a combination of a cyclooxygenase-2 selective inhibitor and a colds and cough active ingredient, and compositions thereof

INVENTOR(S): MacMillan, Stephen P.

PATENT ASSIGNEE(S): Pharmacia Corporation, USA

SOURCE: PCT Int. Appl., 147 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|---|----------|-----------------|------------|
| WO 2003065988 | A2 | 20030814 | WO 2003-US3221 | 20030204 |
| WO 2003065988 | A3 | 20040219 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2474016 | AA | 20030814 | CA 2003-2474016 | 20030204 |
| AU 2003208967 | A1 | 20030902 | AU 2003-208967 | 20030204 |
| US 2004029864 | A1 | 20040212 | US 2003-357747 | 20030204 |
| EP 1471872 | A2 | 20041103 | EP 2003-707692 | 20030204 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| BR 2003007755 | A | 20041207 | BR 2003-7755 | 20030204 |
| JP 2005519923 | T2 | 20050707 | JP 2003-565414 | 20030204 |
| PRIORITY APPLN. INFO.: | | | US 2002-354135P | P 20020204 |
| | | | WO 2003-US3221 | W 20030204 |
| AB | A method for the treatment, prevention and amelioration of colds and/or cough in a subject in need of such treatment, prevention and amelioration, comprises administering to the subject a cyclooxygenase-2 selective inhibitor (e.g. celecoxib; preparation given), or prodrug thereof, and one or more colds and cough active ingredient. Compns., pharmaceutical compns. and kits for practicing the method are also disclosed. | | | |

L8 ANSWER 33 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:570770 CAPLUS

DOCUMENT NUMBER: 139:111710

TITLE: Combinations of peroxisome proliferator-activated receptor- α agonists and cyclooxygenase-2 selective inhibitors, and therapeutic uses therefor
 INVENTOR(S): Obukowicz, Mark G.
 PATENT ASSIGNEE(S): Pharmacia Corporation, USA
 SOURCE: PCT Int. Appl., 155 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 2003059294 | A2 | 20030724 | WO 2003-US956 | 20030114 |
| WO 2003059294 | A3 | 20050714 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2003212138 | A1 | 20031113 | US 2003-341217 | 20030113 |
| CA 2472168 | AA | 20030724 | CA 2003-2472168 | 20030114 |
| AU 2003207535 | A1 | 20030730 | AU 2003-207535 | 20030114 |
| AU 2003207535 | A2 | 20030730 | | |
| JP 2005525313 | T2 | 20050825 | JP 2003-559459 | 20030114 |
| EP 1569640 | A2 | 20050907 | EP 2003-705746 | 20030114 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| CN 1771034 | A | 20060510 | CN 2003-805942 | 20030114 |
| PRIORITY APPLN. INFO.: | | | US 2002-348297P | P 20020114 |
| | | | US 2003-341217 | A 20030113 |
| | | | WO 2003-US956 | W 20030114 |

OTHER SOURCE(S): MARPAT 139:111710

AB Methods for the treatment, prevention, or inhibition of pain, inflammation, or an inflammation-related disorder, and for the treatment or inhibition of a cardiovascular disease or disorder, and for the treatment or inhibition of cancer, and for the treatment of Alzheimer's disease in a subject in need of such treatment, prevention, or inhibition, include treating the subject with a peroxisome proliferator activated receptor- α agonist and a cyclooxygenase-2 selective inhibitor (e.g. celecoxib; preparation described), or prodrug thereof. Compns., pharmaceutical compns., and kits for effecting the particular methods are also described.

L8 ANSWER 34 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:570750 CAPLUS

DOCUMENT NUMBER: 139:111706

TITLE: peroxisome proliferator-activated receptor- α agonist- and cyclooxygenase-2 selective inhibitor-containing compositions, and methods of treatment using them

INVENTOR(S): Needleman, Philip

PATENT ASSIGNEE(S): Pharmacia Corporation, USA

SOURCE: PCT Int. Appl., 157 pp.

CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| WO 2003059271 | A2 | 20030724 | WO 2003-US1099 | 20030114 |
| WO 2003059271 | A3 | 20031127 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF,
BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2003220374 | A1 | 20031127 | US 2003-341174 | 20030113 |
| CA 2472199 | AA | 20030724 | CA 2003-2472199 | 20030114 |
| AU 2003207557 | A1 | 20030730 | AU 2003-207557 | 20030114 |
| AU 2003207557 | A2 | 20030730 | | |
| EP 1465621 | A2 | 20041013 | EP 2003-705768 | 20030114 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| CN 1642544 | A | 20050720 | CN 2003-805886 | 20030114 |
| BR 2003006872 | A | 20050906 | BR 2003-6872 | 20030114 |
| JP 2006501136 | T2 | 20060112 | JP 2003-559436 | 20030114 |
| ZA 2004005562 | A | 20051004 | ZA 2004-5562 | 20040713 |
| PRIORITY APPLN. INFO.: | | | | |
| US 2002-348298P P 20020114 | | | | |
| US 2003-341174 A 20030113 | | | | |
| WO 2003-US1099 W 20030114 | | | | |

OTHER SOURCE(S): MARPAT 139:111706

AB Methods for the treatment, prevention, or inhibition of pain, inflammation, or inflammation-related disorder, and for the treatment or inhibition of a cardiovascular disease or disorder, and for the treatment or inhibition of cancer in a subject in need of such treatment, prevention, or inhibition, include treating the subject with a peroxisome proliferator activated receptor- α agonist and a cyclooxygenase-2 selective inhibitor (e.g. celecoxib; preparation described), or prodrug thereof. Compns., pharmaceutical compns., and kits for effecting the particular methods are also described.

L8 ANSWER 35 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2003:551339 . CAPLUS
 DOCUMENT NUMBER: 139:95464
 TITLE: Treatment of pain, inflammation, and
inflammation-related disorders with a combination of a
cyclooxygenase-2 selective inhibitor and aspirin
 INVENTOR(S): Macmillan, Stephen P.
 PATENT ASSIGNEE(S): Pharmacia Corporation, USA
 SOURCE: PCT Int. Appl., 123 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 2
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|--|----------|-----------------|------------|
| WO 2003057166 | A2 | 20030717 | WO 2003-US255 | 20030107 |
| WO 2003057166 | A3 | 20031106 | | |
| W: | AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | |
| RW: | GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, SE, SI, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | |
| CA 2471951 | AA | 20030717 | CA 2003-2471951 | 20030107 |
| AU 2003207453 | A1 | 20030724 | AU 2003-207453 | 20030107 |
| AU 2003207453 | A2 | 20030724 | | |
| US 2003143271 | A1 | 20030731 | US 2003-337583 | 20030107 |
| US 2003207846 | A1 | 20031106 | US 2003-337760 | 20030107 |
| EP 1469846 | A2 | 20041027 | EP 2003-705660 | 20030107 |
| R: | AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | |
| BR 2003006777 | A | 20050426 | BR 2003-6777 | 20030107 |
| CN 1638760 | A | 20050713 | CN 2003-805349 | 20030107 |
| JP 2005524618 | T2 | 20050818 | JP 2003-557525 | 20030107 |
| ZA 2004005379 | A | 20050617 | ZA 2004-5379 | 20040706 |
| PRIORITY APPLN. INFO.: | | | US 2002-346560P | P 20020107 |
| | | | WO 2003-US255 | W 20030107 |

AB A method for the prevention, treatment, or amelioration of pain, inflammation, or inflammation-related disorder in a subject that is in need of such prevention, treatment or amelioration, involves the administration to the subject of a cyclooxygenase-2 selective inhibitor or prodrug thereof and enteric-coated aspirin. A method can also involve the administration of a cyclooxygenase-2 selective inhibitor and aspirin in an amount lower than 75 mg/day. A method can also involve the administration of a cyclooxygenase-2 selective inhibitor and aspirin where the cyclooxygenase-2 selective inhibitor is BMS-347070, S-33516, CS-502, darbufelone, LAS 34475, LAS 34556, L-745337, SD-8381, RWJ-63556, L-784512, COX-189, ABT-963, or valdecoxib, or any pharmaceutical salt or prodrug thereof. Comps., pharmaceutical compns., and kits that can be used with the methods are also described. Preparation of celecoxib is described.

L8 ANSWER 36 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:532347 CAPLUS

DOCUMENT NUMBER: 139:79173

TITLE: Methods and compositions using a cyclooxygenase 2 (COX-2) inhibitor for the treatment of psychiatric disorders

INVENTOR(S): Muller, Norbert

PATENT ASSIGNEE(S): Germany

SOURCE: U.S. Pat. Appl. Publ., 27 pp.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 3

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------|------|------|-----------------|------|
| | | | | |

| | | | | |
|--|----|----------|------------------|-------------|
| US 2003130334 | A1 | 20030710 | US 2002-157969 | 20020531 |
| EP 1627639 | A2 | 20060222 | EP 2005-24864 | 20020531 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| US 2006167074 | A1 | 20060727 | US 2005-320757 | 20051230 |
| PRIORITY APPLN. INFO.: | | | | |
| | | | DE 2001-10129328 | A 20010619 |
| | | | US 2002-364904P | P 20020314 |
| | | | DE 2001-10129320 | A 20010619 |
| | | | EP 2002-738138 | A3 20020531 |
| | | | US 2002-157969 | A2 20020531 |

OTHER SOURCE(S): MARPAT 139:79173

AB A method for the prevention, treatment, or inhibition of a psychiatric disorder, in particular schizophrenia, is described which comprises administering a COX-2 inhibitor, or prodrug thereof, to a subject. Moreover, a method for the prevention, treatment, or inhibition of a psychiatric disorder, in particular schizophrenia or a depressive disorder, is disclosed, comprising administering to a subject a COX-2 inhibitor or prodrug thereof in combination with a neuroleptic drug or an antidepressant. Compns. and kits that are suitable for the practice of the method are also described.

L8 ANSWER 37 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:492716 CAPLUS

DOCUMENT NUMBER: 139:63316

TITLE: Methods using a combination of a 3-heteroaryl-2-indolinone and a cyclooxygenase-2 inhibitor for the treatment of neoplasia

INVENTOR(S): Masferrer, Jaime L.; Cherrington, Julie M.; Leahy, Kathleen M.; Zweifel, Ben S.

PATENT ASSIGNEE(S): Pharmacia Corporation, USA

SOURCE: U.S. Pat. Appl. Publ., 66 pp., Cont.-in-part of Appl. No. PCT/US99/30693.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 21

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| US 2003119895 | A1 | 20030626 | US 2002-150546 | 20020516 |
| WO 2000038730 | A2 | 20000706 | WO 1999-US30693 | 19991222 |
| WO 2000038730 | A3 | 20001102 | | |
| W: AE, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, LZ, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW | | | | |
| RW: GH, GM, KE, LS, MW, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, BF, BJ, CF, CG, CI, CM, GA, GN, GW, ML, MR, NE, SN, TD, TG | | | | |
| EP 1522313 | A1 | 20050413 | EP 2004-26577 | 19991222 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, FI, RO, CY | | | | |
| CA 2484324 | AA | 20031127 | CA 2003-2484324 | 20030515 |
| WO 2003097044 | A1 | 20031127 | WO 2003-US15582 | 20030515 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, LZ, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NI, NO, NZ, OM, | | | | |

| | | | | |
|---|----|----------|-----------------|-------------|
| PH, PL, PT, RO, RU, SC, SD, SE, SG, SK, SL, TJ, TM, TN, TR, TT,
TZ, UA, UG, US, UZ, VC, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY,
KG, KZ, MD, RU, TJ, TM, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES,
FI, FR, GB, GR, HU, IE, IT, LU, MC, NL, PT, RO, SE, SI, SK, TR,
BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| AU 2003239494 | A1 | 20031202 | AU 2003-239494 | 20030515 |
| BR 2003010027 | A | 20050215 | BR 2003-10027 | 20030515 |
| EP 1509224 | A1 | 20050302 | EP 2003-734058 | 20030515 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT,
IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, HU, SK | | | | |
| JP 2005530781 | T2 | 20051013 | JP 2004-505043 | 20030515 |
| AU 2004210578 | A1 | 20041007 | AU 2004-210578 | 20040910 |
| PRIORITY APPLN. INFO.: | | | | |
| | | | US 1998-113786P | P 19981223 |
| | | | WO 1999-US30693 | A2 19991222 |
| | | | US 1999-385214 | A 19990827 |
| | | | AU 2000-25936 | A3 19991222 |
| | | | EP 1999-968939 | A3 19991222 |
| | | | US 2002-150546 | A 20020516 |
| | | | WO 2003-US15582 | W 20030515 |

OTHER SOURCE(S) : MARPAT 139:63316

AB The invention provides methods and compns. useful for treatment or prevention of neoplasia by administering a combination comprising a 3-heteroaryl-2-indolinone compound (preparation included) and a COX-2 selective inhibitor. Further provided are compns., pharmaceutical compns., and kits for treatment and prevention of neoplasia.

L8 ANSWER 38 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:154262 CAPLUS

DOCUMENT NUMBER: 138:198610

TITLE: Compositions for the treatment and prevention of pain and inflammation with a cyclooxygenase-2 selective inhibitor and chondroitin sulfate

INVENTOR(S) : Pulaski, Steven P.; Kundel, Susan

PATENT ASSIGNEE(S) : Pharmacia Corporation, USA

SOURCE: PCT Int. Appl., 148 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|--|------|----------|-----------------|----------|
| WO 2003015799 | A1 | 20030227 | WO 2002-US25673 | 20020813 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN,
CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH,
GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR,
LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH,
PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ,
UA, UG, US, UZ, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG,
CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL,
PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR,
NE, SN, TD, TG | | | | |
| US 2003114416 | A1 | 20030619 | US 2002-215539 | 20020809 |
| CA 2457452 | AA | 20030227 | CA 2002-2457452 | 20020813 |
| AU 2002336344 | A2 | 20030303 | AU 2002-336344 | 20020813 |
| EP 1416941 | A1 | 20040512 | EP 2002-773188 | 20020813 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, | | | | |

| | | | | |
|--|----|----------|-----------------|------------|
| IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| BR 2002011977 | A | 20040921 | BR 2002-11977 | 20020813 |
| JP 2005501850 | T2 | 20050120 | JP 2003-520758 | 20020813 |
| CN 1575182 | A | 20050202 | CN 2002-820121 | 20020813 |
| ZA 2004001163 | A | 20050622 | ZA 2004-1163 | 20040212 |
| PRIORITY APPLN. INFO.: | | | US 2001-312211P | P 20010814 |
| | | | US 2002-215539 | A 20020809 |
| | | | WO 2002-US25673 | W 20020813 |

OTHER SOURCE(S): MARPAT 138:198610

AB A method of treating, preventing, or inhibiting pain, inflammation, or inflammation-associated disorder in a subject in need of such treatment or prevention includes treating the subject with chondroitin sulfate and a cyclooxygenase-2 selective inhibitor, or a prodrug thereof, wherein the amount of chondroitin sulfate and the amount of a cyclooxygenase-2 selective inhibitor or a pharmaceutically acceptable salt or prodrug thereof together constitute a pain- or inflammation-suppressing treatment or prevention effective amount. Glucosamine can optionally be present. Compns. that contain the combination of chondroitin sulfate and cyclooxygenase-2 selective inhibitor and, optionally, the glucosamine, are disclosed, as are pharmaceutical compns.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 39 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:154260 CAPLUS

DOCUMENT NUMBER: 138:198609

TITLE: Compositions for the treatment and prevention of pain and inflammation with a cyclooxygenase-2 selective inhibitor and glucosamine

INVENTOR(S): Pulaski, Steven P.; Kundel, Susan

PATENT ASSIGNEE(S): Pharmacia Corporation, USA

SOURCE: PCT Int. Appl., 145 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|----------|
| WO 2003015797 | A1 | 20030227 | WO 2002-US25674 | 20020813 |
| WO 2003015797 | C1 | 20041229 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 2003114418 | A1 | 20030619 | US 2002-215816 | 20020809 |
| CA 2457453 | AA | 20030227 | CA 2002-2457453 | 20020813 |
| AU 2002331076 | A2 | 20030303 | AU 2002-331076 | 20020813 |
| EP 1416940 | A1 | 20040512 | EP 2002-768522 | 20020813 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| BR 2002011936 | A | 20041026 | BR 2002-11936 | 20020813 |

| | | | | |
|------------------------|----|----------|-----------------|------------|
| JP 2005507871 | T2 | 20050324 | JP 2003-520756 | 20020813 |
| CN 1767835 | A | 20060503 | CN 2002-820216 | 20020813 |
| ZA 2004001158 | A | 20050622 | ZA 2004-1158 | 20040212 |
| PRIORITY APPLN. INFO.: | | | US 2001-312272P | P 20010814 |
| | | | US 2002-215216 | A 20020809 |
| | | | US 2002-215816 | A 20020809 |
| | | | WO 2002-US25674 | W 20020813 |

OTHER SOURCE(S): MARPAT 138:198609

AB A method of treating, preventing, or inhibiting pain, inflammation or inflammation-associated disorder in a subject in need of such treatment or prevention provides for treating the subject with glucosamine and a cyclooxygenase-2 selective inhibitor or prodrug thereof, wherein the amount of glucosamine and the amount of a cyclooxygenase-2 selective inhibitor or prodrug thereof together constitute a pain or inflammation suppressing treatment or prevention effective amount of the composition Compns. and pharmaceutical compns. that contain glucosamine and a cyclooxygenase-2 selective inhibitor are also disclosed.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 40 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2003:154230 CAPLUS

DOCUMENT NUMBER: 138:210277

TITLE: Synthesis and use of reagents for improved DNA lipofection and/or slow release prodrug and drug therapies

INVENTOR(S): Diamond, Scott L.; Gruneich, Jeffrey

PATENT ASSIGNEE(S): The Trustees of the University of Pennsylvania, USA

SOURCE: PCT Int. Appl., 70 pp.

CODEN: PIXXD2

DOCUMENT TYPE: Patent

LANGUAGE: English

FAMILY ACC. NUM. COUNT: 1

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 2003015757 | A1 | 20030227 | WO 2002-US26152 | 20020815 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AT, BE, BG, CH, CY, CZ, DE, DK, EE, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, SK, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2456977 | AA | 20030227 | CA 2002-2456977 | 20020815 |
| EP 1424998 | A1 | 20040609 | EP 2002-759383 | 20020815 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR, BG, CZ, EE, SK | | | | |
| JP 2005525290 | T2 | 20050825 | JP 2003-520717 | 20020815 |
| US 2005069577 | A1 | 20050331 | US 2004-777805 | 20040212 |
| PRIORITY APPLN. INFO.: | | | US 2001-312729P | P 20010816 |
| | | | US 2002-358138P | P 20020220 |
| | | | WO 2002-US26152 | W 20020815 |

AB The invention relates to compns. and methods for a one-step synthetic technique for making cationic steroid or cationic drug mols. for use as delivery vehicles. The invention further relates to methods for using

cationic steroid mols. in lipofection or transfection, delivery of drugs, and for treatment of inflammation and other diseases and disorders. The invention also relates to cationic steroid prodrugs and cationic prodrugs and to methods of modifying drugs.

REFERENCE COUNT: 4 THERE ARE 4 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 41 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2002:977588 CAPLUS
 DOCUMENT NUMBER: 138:33362
 TITLE: Use of cyclooxygenase 2 (COX-2) inhibitors for the treatment of schizophrenia, delusional disorders, affective disorders, autism, or tic disorders
 INVENTOR(S): Muller, Norbert
 PATENT ASSIGNEE(S): Germany
 SOURCE: PCT Int. Appl., 58 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 3
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|------------------|-------------|
| WO 2002102297 | A2 | 20021227 | WO 2002-EP6013 | 20020531 |
| WO 2002102297 | A3 | 20030501 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| DE 10129320 | A1 | 20030410 | DE 2001-10129320 | 20010619 |
| CA 2448025 | AA | 20021227 | CA 2002-2448025 | 20020531 |
| EP 1397145 | A2 | 20040317 | EP 2002-738138 | 20020531 |
| EP 1397145 | B1 | 20060906 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| JP 2004534066 | T2 | 20041111 | JP 2003-504886 | 20020531 |
| EP 1627639 | A2 | 20060222 | EP 2005-24864 | 20020531 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| US 2004204469 | A1 | 20041014 | US 2004-480600 | 20040205 |
| PRIORITY APPLN. INFO.: | | | DE 2001-10129320 | A 20010619 |
| | | | US 2002-364904P | P 20020314 |
| | | | EP 2002-738138 | A3 20020531 |
| | | | WO 2002-EP6013 | W 20020531 |

OTHER SOURCE(S): MARPAT 138:33362

AB The invention discloses the use of a COX-2 inhibitor for the treatment of psychiatric disorders, e.g. schizophrenia, delusional disorders, affective disorders, autism or tic disorders, in particular chronic schizophrenic psychoses and schizoaffective psychoses, temporary acute psychotic disorders, depressive episodes, recurring depressive episodes, manic episodes and bipolar affective disorders. Moreover, the invention discloses the use of a COX-2 inhibitor, in particular celecoxib, in combination with a neuroleptic drug, in particular risperidone, or an

antidepressant, for the treatment of psychiatric disorders such as schizophrenia, delusional disorders, affective disorders, autism or tic disorders.

L8 ANSWER 42 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2002:927258 CAPLUS
 DOCUMENT NUMBER: 138:16609
 TITLE: Skin-permeable selective cyclooxygenase-2 inhibitor composition
 INVENTOR(S): Lu, Guang Wei; Ewing, Gary D.; Tyle, Praveen; Stoller, Brenda M.; Gokhale, Rajeev; Gadre, Ashwini
 PATENT ASSIGNEE(S): Pharmacia Corporation, USA
 SOURCE: PCT Int. Appl., 55 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 4
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 2002096435 | A2 | 20021205 | WO 2002-US17067 | 20020530 |
| WO 2002096435 | A3 | 20030501 | | |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| CA 2448627 | AA | 20021205 | CA 2002-2448627 | 20020530 |
| US 2003161867 | A1 | 20030828 | US 2002-158342 | 20020530 |
| NZ 529797 | A | 20031219 | NZ 2002-529797 | 20020530 |
| EP 1404345 | A2 | 20040407 | EP 2002-774123 | 20020530 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| BR 2002010104 | A | 20040608 | BR 2002-10104 | 20020530 |
| JP 2004532871 | T2 | 20041028 | JP 2002-592944 | 20020530 |
| CN 1547474 | A | 20041117 | CN 2002-814946 | 20020530 |
| ZA 2003009298 | A | 20040512 | ZA 2003-9298 | 20031128 |
| PRIORITY APPLN. INFO.: | | | US 2001-294838P | P 20010531 |
| | | | US 2001-350756P | P 20011113 |
| | | | WO 2002-US17067 | W 20020530 |

OTHER SOURCE(S): MARPAT 138:16609

AB A skin deliverable pharmaceutical composition comprises at least 1 selective cyclooxygenase-2 (COX-2) inhibitory drug or prodrug thereof solubilized in a pharmaceutically acceptable carrier that contains a low mol. weight monohydric alc., and exhibits a skin permeation rate of the therapeutic agent at least equal to that exhibited by a reference solution of the

therapeutic agent in 70% aqueous ethanol. A method of effecting targeted delivery of a selective COX-2 inhibitory drug to a site of pain and/or inflammation in a subject comprises topically administering such a composition to skin of the subject, preferably at a locus overlying or adjacent to the site of pain and/or inflammation. A method of effecting systemic treatment of a subject having a COX-2 mediated disorder comprises transdermally administering such a composition, preferably by contacting the

composition with an area of skin of the subject ≥ 400 cm². Thus, celecoxib was observed in 70% aqueous EtOH and this solution provided greater skin flux of the drug.

L8 ANSWER 43 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 2002:556104 CAPLUS
 DOCUMENT NUMBER: 137:109489
 TITLE: Compositions comprising a polypeptide and an active agent
 INVENTOR(S): Piccariello, Thomas; Olon, Lawrence P.; Kirk, Randal J.
 PATENT ASSIGNEE(S): USA
 SOURCE: U.S. Pat. Appl. Publ., 34 pp.
 CODEN: USXXCO
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 20
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|------------|
| US 2002099013 | A1 | 20020725 | US 2001-933708 | 20010822 |
| US 2004087483 | A1 | 20040506 | US 2002-136433 | 20020502 |
| US 2004063628 | A1 | 20040401 | US 2002-156527 | 20020529 |
| US 7060708 | B2 | 20060613 | | |
| US 2006014697 | A1 | 20060119 | US 2005-89056 | 20050325 |
| PRIORITY APPLN. INFO.: | | | | |
| | | | US 2000-247556P | P 20001114 |
| | | | US 2000-247558P | P 20001114 |
| | | | US 2000-247559P | P 20001114 |
| | | | US 2000-247560P | P 20001114 |
| | | | US 2000-247561P | P 20001114 |
| | | | US 2000-247594P | P 20001114 |
| | | | US 2000-247595P | P 20001114 |
| | | | US 2000-247606P | P 20001114 |
| | | | US 2000-247607P | P 20001114 |
| | | | US 2000-247608P | P 20001114 |
| | | | US 2000-247609P | P 20001114 |
| | | | US 2000-247610P | P 20001114 |
| | | | US 2000-247611P | P 20001114 |
| | | | US 2000-247612P | P 20001114 |
| | | | US 2000-247620P | P 20001114 |
| | | | US 2000-247621P | P 20001114 |
| | | | US 2000-247634P | P 20001114 |
| | | | US 2000-247635P | P 20001114 |
| | | | US 2000-247698P | P 20001114 |
| | | | US 2000-247699P | P 20001114 |
| | | | US 2000-247700P | P 20001114 |
| | | | US 2000-247701P | P 20001114 |
| | | | US 2000-247702P | P 20001114 |
| | | | US 2000-247797P | P 20001114 |
| | | | US 2000-247798P | P 20001114 |
| | | | US 2000-247799P | P 20001114 |
| | | | US 2000-247800P | P 20001114 |
| | | | US 2000-247801P | P 20001114 |
| | | | US 2000-247802P | P 20001114 |
| | | | US 2000-247803P | P 20001114 |
| | | | US 2000-247804P | P 20001114 |
| | | | US 2000-247805P | P 20001114 |
| | | | US 2000-247807P | P 20001114 |

| | |
|-----------------|-------------|
| US 2000-247832P | P 20001114 |
| US 2000-247833P | P 20001114 |
| US 2000-247926P | P 20001114 |
| US 2000-247927P | P 20001114 |
| US 2000-247928P | P 20001114 |
| US 2000-247929P | P 20001114 |
| US 2000-247930P | P 20001114 |
| US 1999-265415 | B2 19990310 |
| US 1999-411238 | B2 19991004 |
| WO 2000-US5693 | A 20000306 |
| US 2000-642820 | A2 20000822 |
| US 2000-248607P | P 20001116 |
| US 2000-248620P | P 20001116 |
| US 2000-248656P | P 20001116 |
| US 2000-248658P | P 20001116 |
| US 2000-248659P | P 20001116 |
| US 2000-248660P | P 20001116 |
| US 2000-248662P | P 20001116 |
| US 2000-248663P | P 20001116 |
| US 2000-248685P | P 20001116 |
| US 2000-248737P | P 20001116 |
| US 2000-248738P | P 20001116 |
| US 2000-248764P | P 20001116 |
| US 2000-248767P | P 20001116 |
| US 2000-248768P | P 20001116 |
| US 2000-248769P | P 20001116 |
| US 2000-248770P | P 20001116 |
| US 2000-248771P | P 20001116 |
| US 2000-248772P | P 20001116 |
| US 2000-248774P | P 20001116 |
| US 2000-248776P | P 20001116 |
| US 2000-248777P | P 20001116 |
| US 2000-248778P | P 20001116 |
| US 2000-248779P | P 20001116 |
| US 2000-248782P | P 20001116 |
| US 2000-248787P | P 20001116 |
| US 2000-248794P | P 20001116 |
| US 2000-248795P | P 20001116 |
| US 2000-248796P | P 20001116 |
| US 2000-248797P | P 20001116 |
| US 2001-933708 | A2 20010822 |
| US 2001-986426 | A2 20011108 |
| US 2001-987458 | B2 20011114 |
| WO 2001-US43089 | B2 20011114 |
| US 2001-988034 | B2 20011116 |
| US 2001-988071 | B2 20011116 |
| WO 2001-US43115 | B2 20011116 |
| WO 2001-US43117 | B2 20011116 |
| US 2002-358368P | P 20020222 |
| US 2002-358381P | P 20020222 |
| US 2002-362082P | P 20020307 |
| US 2002-366258P | P 20020322 |
| US 2002-156527 | A2 20020529 |
| WO 2003-US5525 | A2 20030224 |
| US 2003-507012P | P 20030930 |
| US 2004-567800P | P 20040505 |
| US 2004-567802P | P 20040505 |
| US 2004-568011P | P 20040505 |
| US 2004-923088 | A2 20040823 |
| US 2004-923257 | A2 20040823 |

| | |
|-----------------|-------------|
| US 2004-953110 | A2 20040930 |
| US 2004-953111 | A2 20040930 |
| US 2004-953116 | A2 20040930 |
| US 2004-953119 | A2 20040930 |
| US 2004-955006 | A2 20040930 |
| WO 2004-US32131 | A2 20040930 |

AB Claimed are compns. comprising a polypeptide and an active agent covalently attached to the polypeptide and a method for delivery of an active agent to a patient by administering the composition to the patient. The peptide is a homopolymer of a naturally occurring amino acid or a heteropolymer of two or more naturally occurring amino acids. In an example, (Glu)_n-cephalexin was prepared from Glu(OBut)NCA and cephalixin hydrochloride.

L8 ANSWER 44 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:392237 CAPLUS

DOCUMENT NUMBER: 136:401651

TITLE: Preparation of fused pyridine derivatives as HMG-CoA reductase inhibitors

INVENTOR(S): Robl, Jeffrey A.; Chen, Bang-Chi; Sun, Chong-Qing

PATENT ASSIGNEE(S): USA

SOURCE: U.S. Pat. Appl. Publ., 46 pp., Cont.-in-part of U.S. Ser. No. 875,218.

CODEN: USXXCO

DOCUMENT TYPE: Patent

LANGUAGE: English

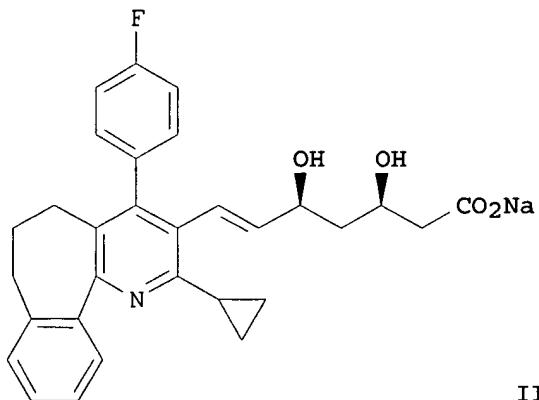
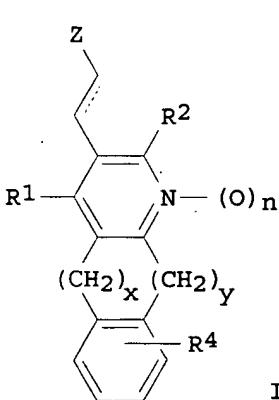
FAMILY ACC. NUM. COUNT: 2

PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|------|----------|-----------------|-------------|
| US 2002061901 | A1 | 20020523 | US 2001-8154 | 20011204 |
| US 6620821 | B2 | 20030916 | | |
| US 2002028826 | A1 | 20020307 | US 2001-875218 | 20010606 |
| US 2004024216 | A1 | 20040205 | US 2003-602753 | 20030624 |
| PRIORITY APPLN. INFO.: | | | US 2000-211594P | P 20000615 |
| | | | US 2001-875218 | A2 20010606 |
| | | | US 2001-8154 | A3 20011204 |

OTHER SOURCE(S): MARPAT 136:401651

GI



AB The title compds. I and their pharmaceutically acceptable salts, esters, prodrug esters, and stereoisomers are claimed [wherein: Z = CH(OH)CH₂CR₇(OH)CH₂CO₂R₃ or corresponding pyranone lactone derivs.; n = 0, 1; x = 0, 1, 2, 3, or 4; y = 0, 1, 2, 3 or 4, provided that at least one of x and y is other than 0; and optionally one or more carbons of (CH₂)_x and/or (CH₂)_y together with addnl. carbons form a 3 to 7 membered spirocyclic ring; R₁, R₂ = alkyl, arylalkyl, cycloalkyl, alkenyl, cycloalkenyl, aryl, heteroaryl, cycloheteroalkyl; R₃ = H or lower alkyl; R₄ = H, halo, CF₃, OH, alkyl, alkoxy, CO₂H, (un)substituted NH₂, cyano, (un)substituted CONH₂, etc.; R₇ = H, alkyl]. The compds. are HMG-CoA reductase inhibitors, and are active in inhibiting cholesterol biosynthesis and modulating blood serum lipids, for example, lowering LDL cholesterol and/or increasing HDL cholesterol (no data). They are thus useful in treating hyperlipidemia and dyslipidemia, in hormone replacement therapy, and in treating hypercholesterolemia, hypertriglyceridemia and atherosclerosis, as well as Alzheimer's disease and osteoporosis. Preps. of several compds. are described. For instance, a multistep synthesis of fused pyridine derivative II is reported. Compds. I may be used in a manner similar to atorvastatin, pravastatin, simvastatin, etc. Combinations of compds. I with various other drugs are claimed, the latter being specified as certain pharmacol. classes, as inhibitors of specific enzymes, as (ant)agonists of specific receptors, and as numerous named drugs.

L8 ANSWER 45 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:332011 CAPLUS
 DOCUMENT NUMBER: 136:355482
 TITLE: Compositions comprising a polypeptide and an active agent
 INVENTOR(S): Piccariello, Thomas; Olon, Lawrence P.; Kirk, Randall J.
 PATENT ASSIGNEE(S): New River Pharmaceuticals, Inc., USA
 SOURCE: PCT Int. Appl., 98 pp.
 CODEN: PIXXD2
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 20
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| WO 2002034237 | A1 | 20020502 | WO 2001-US26142 | 20010822 |
| W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, UZ, VN, YU, ZA, ZW | | | | |
| RW: GH, GM, KE, LS, MW, MZ, SD, SL, SZ, TZ, UG, ZW, AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE, TR, BF, BJ, CF, CG, CI, CM, GA, GN, GQ, GW, ML, MR, NE, SN, TD, TG | | | | |
| US 6716452 | B1 | 20040406 | US 2000-642820 | 20000822 |
| CA 2420590 | AA | 20020502 | CA 2001-2420590 | 20010822 |
| AU 2001086599 | A5 | 20020506 | AU 2001-86599 | 20010822 |
| EP 1311242 | A1 | 20030521 | EP 2001-966056 | 20010822 |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO, MK, CY, AL, TR | | | | |
| JP 2004523480 | T2 | 20040805 | JP 2002-537291 | 20010822 |
| US 2004127397 | A1 | 20040701 | US 2003-727565 | 20031205 |
| PRIORITY APPLN. INFO.: | | | US 2000-642820 | A 20000822 |

| | | |
|-----------------|---|----------|
| US 2000-247613P | P | 20001114 |
| US 2000-247614P | P | 20001114 |
| US 2000-247615P | P | 20001114 |
| US 2000-247616P | P | 20001114 |
| US 2000-247617P | P | 20001114 |
| US 2000-247622P | P | 20001114 |
| US 2000-247630P | P | 20001114 |
| US 2000-247631P | P | 20001114 |
| US 2000-247632P | P | 20001114 |
| US 2000-247633P | P | 20001114 |
| US 2000-247556P | P | 20001114 |
| US 2000-247558P | P | 20001114 |
| US 2000-247559P | P | 20001114 |
| US 2000-247560P | P | 20001114 |
| US 2000-247561P | P | 20001114 |
| US 2000-247594P | P | 20001114 |
| US 2000-247595P | P | 20001114 |
| US 2000-247606P | P | 20001114 |
| US 2000-247607P | P | 20001114 |
| US 2000-247608P | P | 20001114 |
| US 2000-247609P | P | 20001114 |
| US 2000-247610P | P | 20001114 |
| US 2000-247611P | P | 20001114 |
| US 2000-247612P | P | 20001114 |
| US 2000-247620P | P | 20001114 |
| US 2000-247621P | P | 20001114 |
| US 2000-247634P | P | 20001114 |
| US 2000-247635P | P | 20001114 |
| US 2000-247698P | P | 20001114 |
| US 2000-247699P | P | 20001114 |
| US 2000-247701P | P | 20001114 |
| US 2000-247702P | P | 20001114 |
| US 2000-247797P | P | 20001114 |
| US 2000-247798P | P | 20001114 |
| US 2000-247799P | P | 20001114 |
| US 2000-247800P | P | 20001114 |
| US 2000-247801P | P | 20001114 |
| US 2000-247802P | P | 20001114 |
| US 2000-247803P | P | 20001114 |
| US 2000-247804P | P | 20001114 |
| WO 2001-US26142 | W | 20010822 |

AB Claimed are compns. comprising a polypeptide and an active agent covalently attached to the polypeptide and a method for delivery of an active agent to a patient by administering the composition to the patient. The peptide is a homopolymer of a naturally occurring amino acid or a heteropolymer of two or more naturally occurring amino acids. In an example, (Glu)n-cephalexin was prepared from Glu(OBut)NCA and cephalexin hydrochloride.

REFERENCE COUNT: 11 THERE ARE 11 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 46 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:327387 CAPLUS
DOCUMENT NUMBER: 137:332985
TITLE: Superior analgesic effect of loxoprofen Na, a prodrug of a non-selective COX inhibitor, over COX-2 selective inhibitors in rats
AUTHOR(S): Makino, Mitsuko; Kojima, Takayoshi; Hayakawa, Makiko; Hiramoto, Kumiko; Mori, Masayoshi
CORPORATE SOURCE: International Product Management & Medical Affairs

SOURCE: Department, Sankyo Co., Ltd., Tokyo, 103-8426, Japan
Annual Report of Sankyo Research Laboratories (2001),
53, 103-108

PUBLISHER: CODEN: ASRLEC; ISSN: 1341-741X
Sankyo Co., Ltd., Research Institute
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The analgesic effect of loxoprofen Na, a prodrug of a non-selective COX inhibitor, was compared with indomethacin, a non-selective COX inhibitor, and selective COX-2 inhibitors such as celecoxib, rofecoxib and meloxicam by using the Randall-Selitto method in rats. Loxoprofen Na suppressed pain sensation at doses of 0.13 mg/kg and higher, while indomethacin, celecoxib, rofecoxib and meloxicam suppressed this at doses of 8.4, 0.98, 2.4 and 18.3 mg/kg, resp., and higher. Judging from the min. EDs, loxoprofen Na seems to have 7-140 times more potent analgesic action than the selective COX-2 inhibitors and indomethacin. Furthermore, the analgesic activity of loxoprofen Na appeared 15 min after oral administration, which was the shortest latency among the NSAIDs examined. Although loxoprofen Na is a prodrug, its rapid oral absorption and conversion to the active form (trans-OH metabolite), which have been already reported, would explain the short latency to the appearance of its analgesic action. This is the first manuscript to report comparison of the analgesic action of a prodrug of a non-selective COX inhibitor with that of selective COX-2 inhibitors in rats. The present data indicates that the analgesic effect of loxoprofen Na is superior to the COX-2 selective inhibitors examined

REFERENCE COUNT: 13 THERE ARE 13 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L8 ANSWER 47 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2002:276519 CAPLUS
DOCUMENT NUMBER: 136:310188
TITLE: Treatment of cancer with a prostate specific antigen (PSA) conjugate and an NSAID compound
INVENTOR(S): Heimbrook, David C.; Yao, Siu-long
PATENT ASSIGNEE(S): USA
SOURCE: U.S. Pat. Appl. Publ., 129 pp.
CODEN: USXXCO
DOCUMENT TYPE: Patent
LANGUAGE: English
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|-------|----------|-----------------|------------|
| ----- | ----- | ----- | ----- | ----- |
| US 2002042375 | A1 | 20020411 | US 2001-896245 | 20010629 |
| PRIORITY APPLN. INFO.: | | | US 2000-216217P | P 20000705 |

OTHER SOURCE(S): MARPAT 136:310188

AB The invention relates to methods of treating cancer using a combination of a compound which is a PSA conjugate and a nonsteroidal antiinflammatory agent (NSAID) and to methods of preparing such compns. The PSA conjugate comprises an oligopeptide that is selectively cleaved by PSA and a cytotoxic agent. An example of a PSA conjugate is N-Ac-(4-trans-L-Hyp)-Ala-Ser-Chg-Gln-Ser-Leu-Dox (Dox = doxorubicin, Hyp = hydroxyproline, Chg = cyclohexylglycine) and COX-2 inhibitor 3-phenyl-4-[4-(4-methylsulfonyl)phenyl]-2(5H)furanone is an example of an NSAID compound (syntheses given).

L8 ANSWER 48 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN

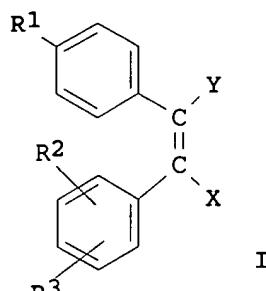
ACCESSION NUMBER: 2001:10616 CAPLUS
 DOCUMENT NUMBER: 134:91125
 TITLE: Pharmaceutical compositions containing aldose reductase inhibitors and selective cyclooxygenase-2 inhibitors
 INVENTOR(S): Mylari, Banavara Lakshman
 PATENT ASSIGNEE(S): Pfizer Products Inc., USA
 SOURCE: Eur. Pat. Appl., 103 pp.
 CODEN: EPXXDW
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|---|------|----------|-----------------|------------|
| EP 1064965 | A2 | 20010103 | EP 2000-305361 | 20000626 |
| EP 1064965 | A3 | 20030212 | | |
| R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO | | | | |
| US 6555540 | B1 | 20030429 | US 2000-602419 | 20000623 |
| JP 2001031569 | A2 | 20010206 | JP 2000-194053 | 20000628 |
| CA 2313063 | AA | 20001230 | CA 2000-2313063 | 20000629 |
| BR 2000002957 | A | 20010130 | BR 2000-2957 | 20000630 |
| PRIORITY APPLN. INFO.: | | | US 1999-141695P | P 19990630 |

OTHER SOURCE(S): MARPAT 134:91125
 AB Pharmaceutical compns. containing aldose reductase inhibitors, a prodrug thereof or a salts and and selective cyclooxygenase-2 inhibitors, a prodrug thereof or salts thereof are disclosed. The compns. are used for the treatment of diabetic complications such as diabetic neuropathy, diabetic nephropathy, diabetic retinopathy and diabetic cardiomyopathy. Hard gelatin capsules contained active ingredients 0.25-100, starch 0.o-650, starch powder 0.o-50, and silicone fluid 350-cSt 0.15 mg/capsules.

L8 ANSWER 49 OF 49 CAPLUS COPYRIGHT 2006 ACS on STN
 ACCESSION NUMBER: 1998:202670 CAPLUS
 DOCUMENT NUMBER: 128:266249
 TITLE: Diphenyl stilbenes as prodrugs to cyclooxygenase-2 inhibitors, pharmaceutical compositions, and preparation thereof
 INVENTOR(S): Black, Cameron; Girard, Mario; Guay, Daniel; Wang, Zhaoyin
 PATENT ASSIGNEE(S): Merck Frosst Canada, Inc., Can.
 SOURCE: U.S., 21 pp.
 CODEN: USXXAM
 DOCUMENT TYPE: Patent
 LANGUAGE: English
 FAMILY ACC. NUM. COUNT: 1
 PATENT INFORMATION:

| PATENT NO. | KIND | DATE | APPLICATION NO. | DATE |
|------------------------|-------------------|----------|-----------------|----------|
| US 5733909 | A | 19980331 | US 1997-784663 | 19970121 |
| PRIORITY APPLN. INFO.: | | | US 1997-784663 | 19970121 |
| OTHER SOURCE(S): | MARPAT 128:266249 | | | |
| GI | | | | |



AB Compds. I [X = CH₂OH, CHO, CO₂R₄, CONR₄; Y = Me, CH₂OR₅; R₁ = S(O)₂Me, S(O)2NH₂, etc.; R₂, R₃ = H, halo, C₁₋₆ alkoxy, etc.; R₄ = H, C₁₋₆ alkyl, etc.; R₅ = C₁₋₆ alkyl, (substituted) benzyl] are disclosed for the treatment of cyclooxygenase-2 mediated diseases. Also disclosed are pharmaceutical compns. containing I for treatment of cyclooxygenase-2 mediated diseases. Compds. of the invention are useful for treating inflammatory diseases susceptible to treatment with a nonsteroidal antiinflammatory agent. Preparation of selected I is described.

REFERENCE COUNT: 3 THERE ARE 3 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

| => log h | | | |
|--|------------|---------|--|
| COST IN U.S. DOLLARS | SINCE FILE | TOTAL | |
| | ENTRY | SESSION | |
| FULL ESTIMATED COST | 137.54 | 332.68 | |
| DISCOUNT AMOUNTS (FOR QUALIFYING ACCOUNTS) | SINCE FILE | TOTAL | |
| | ENTRY | SESSION | |
| CA SUBSCRIBER PRICE | -36.75 | -39.75 | |

SESSION WILL BE HELD FOR 60 MINUTES
STN INTERNATIONAL SESSION SUSPENDED AT 15:49:01 ON 18 SEP 2006